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WOOD'S MEDICAL AND SURGICAL MONOGRAPHS

CONTENTS

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BY WILLIAM JAPP SINCLAIR, M.A., M.D.

ON GIDDINESS
BY THOMAS GRAINGER STEWART, M.D.

ALBUMINURIA IN BRIGHT'S DISEASE
BY DR. PIERRE JAENTON.

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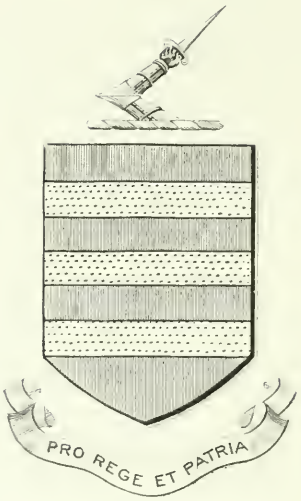

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Medical and Surgical

MONOGRAPHS

Consisting of Original Treatises and of Complete Reproductions, in English, of Books and Monographs selected from the latest literature of foreign countries, with all illustrations, etc.

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ON

GONORRHŒAL INFECTION

IN WOMEN.

BY

WILLIAM JAPP SINCLAIR, M.A., M.D.

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ON GONORRHŒAL INFECTION IN WOMEN.

CHAPTER I.

GONORRHŒAL INFECTION PRODUCES COMPLICATIONS WHICH ARE SERIOUS IN THEMSELVES AND OF FREQUENT OCCURRENCE.

Importance to the Gynæcologist.

Gonorrhœa as it occurs in the female sex is still in this country strangely neglected by general practitioner and specialist alike. Its symptoms, its differential diagnosis, and the ravages which are its immediate or remote results, are hardly recognized or understood, and the treatment of it, as ordinarily practised, is contemptible. Yet the virus of this disorder gives rise to a group of diseases, a series of pathological conditions, which, by reason of their clinical interest and their social and moral consequences, surpass in importance any other class of affections with which the gynæcologist is called upon to deal. To the reader, cognisant of the eager activity which, now as heretofore, pervades every department of medical research and practice, there must appear to be something extreme or paradoxical in this statement. But the explanation is not far to seek. If gonorrhœa stood alone among the diseases of women that had been neglected for generations by the surgeons, the explanation might be difficult; but it has only shared what was the common lot with abdominal and uterine surgery until the latter was removed from the limbo of neglected subjects by the work of the specialists, so recently that many of the early reformers are still alive and engaged in the active practice of their profession. Even yet the importance of the part played by the gonorrhœal

virus in the production of disease has received comparatively little attention from the gynæcologists in England and America, whereas in some other countries, especially in Germany, in recent years, a large amount of experimental work has been done, and much clinical evidence has been collected, which must soon work a revolution in the opinions and practice of the profession throughout the world in regard to certain phases of gonorrhœal disease. So little even of foreign work has been published in England, that it can be no exaggeration to say that if the whole subject could be put before the practitioners of this country in all its fullness of detail, both theoretical and practical, as it has developed in Germany during the last few years, the knowledge would come as a surprise and a revelation. Writing with this conviction, I need hardly apologise for endeavoring to give an outline of these recent researches and observations, especially as I shall be able to incorporate some observations and illustrative cases of my own, which can hardly fail to be recognised as corroborative evidence in support of conclusions already suggested in the opening sentences, and ultimately to be stated more explicitly and formally.

Erroneous and Inadequate Views Taught.

There are few medical practitioners in this country who, when medical students, were not entirely mistaught with regard to the pathology and treatment of gonorrhœa in women. Their teachers were the pure surgeons, and when these taught that the disease was to be considered only a form milder in its course, and more amenable to treatment, when affecting the female sex, there need to be no surprise if the practitioner has carried the ignorance of his teachers into his daily practice, with disastrous consequences to some of his patients. Whether the teaching of an old pathology is still carried on, I do not know; but there is no evidence of a change in some of the most recent works on surgery. It would be interesting, if space permitted, to collate a series of quotations on gonorrhœa in women from the older and more recent manuals of surgery, as exhibiting the barrenness of surgical observation until the subject was taken in hand by the specialists. It must suffice, however, to quote from the article "Gonorrhœa"

in Holmes's "System of Surgery." This work is selected as one which is looked upon by many practitioners as a complete library of surgical literature, and as I quote from the third edition, published in 1883, it may fairly be assumed that we have here a statement of the orthodox surgical doctrine of the present time, as understood by the average general practitioner; and, having it fresh before us, we shall be better able to see how we stand with regard to the orthodox creed when we have assimilated the newer knowledge. Under the subdivision, "Gonorrhœa in the Female," the author says[1]: "Gonorrhœa is a much less common affection in women than in men, and when it does occur, the disease is ordinarily much less severe, and hence more rarely comes under treatment. . . Inflammation, in consequence of gonorrhœa, has been supposed to extend to the cavity of the uterus and to the Fallopian tubes. West mentions two successive attacks of vaginitis, at an interval of eighteen months, in same patient, which were followed by such severe peritonitis as to call on each occasion for the abstraction of blood. . . . Ovarian inflammation, corresponding to the epididymitis of the male, occasionally occurs. It has been described by Hunter, Dr. Tilt, and others."

There is in this chapter not a single expression to convey to the reader any hint of the serious nature of the complications of gonorrhœa in women, as compared with the corresponding phases of the affection in men. The existence of a "latent" or creeping form of the disease is not so much as mentioned, and the author is equally silent with regard to dysmenorrhœa, pyo-salpinx, sterility, and other well-recognised results of the disease. It will be observed that the date of this essay is eleven years later than the appearance of Noeggerath's work; six years later than when Lawson Tait wrote,[2] "Acute ovaritis from gonorrhœa is a common result of the infection;" and four years after Neisser's first publication on the discovery of the gonococcus. It need not surprise us if the practical outcome of such teaching is a very lame method of dealing with the disease in the male, with unfortunate results for the female. The ordinary treatment of the male sex, with its consequences, is well illustrated by a case at present under my care, which,

[1] "A System of Surgery, by various Authors." Edited by Holmes; p. 391, 3rd Edition, 1883.

[2] "Diseases of Women, 1877.

in its clinical aspect, as affecting the woman, will be given in more detail in the sequel. It is that of an hospital patient, suffering from acute pelvic inflammation, as I shall call it at present, the special internal development of the disease not having been as yet sufficiently differentiated. She has been married only about two months, and she has a turbid uterine discharge, which has been ascertained to contain gonococci in abundance. In order, if possible, to obtain corroborative evidence, without too closely questioning the wife, I sent for the husband. I told him my object in wishing to speak with him was to learn if he had had clap? "Yes, I had," said he, quite frankly. "When?" "I got it in August last year." "When were you cured?" "In November." "When did you get married?" "In the beginning of February." "When did your wife begin to complain?" "Last month"—that is, in March, just about a month after marriage. In answer to further questions, my interlocutor informed me that the doctor who treated him first, considered him quite cured in November. There was some uneasiness in the genitals about Christmas, and he consulted another practitioner, with special reference to the question of marriage at an early date. Although the patient was the subject of phimosis, and his glans could not be seen, he was assured that he was all right, and might get married without misgiving. Very soon after marriage he began to have a discharge, and his wife became ill, complaining of intense hypogastric pain, which necessitated her taking to bed. Still another medical practitioner was called in to attend the wife, and he was also consulted by the husband on account of some symptoms which had reappeared. This doctor recommended, and performed, the operation of circumcision on the husband, and is reported to have assured him that there was no sort of connection between his wife's ailment and his own. The final result in this case, so far, is a gleet in the husband, and an ailment which is probably destined to do irretrievable damage to the sexual organs, and perhaps to the general health, of the wife.

In further illustration of the practice which may result from an inadequate apprehension of the danger to women arising from gonorrhœal infection, I shall quote from a comparatively recent French writer on the venereal diseases. Speaking of the case of a young man about to be married, who has had

the misfortune to contract a gonorrhœa which there is not time to cure before the wedding day, he says: "In these embarrassing circumstances, one sovereign remedy remains, only one—injections of nitrate of silver. . . . Suppose one employs a medium dose of the solution, in an hour and a half or two hours after the injection there appears a discharge, the simple effect of traumatism, accompanied by a little smarting in micturition. This slight inflammation lasts five or six hours. But then, precious result, the canal becomes dry; all morbid secretion is arrested, and this condition persists for eighteen or twenty-four hours—quite sufficient time for the bridegroom to seek his nuptial couch in a healthy, or, at least, noncontagious state. In exact figures, if the newly-wedded pair ought to retire to their room on Friday morning at one o'clock, the preservative injection ought to be made about nine o'clock on Thursday forenoon."[1] This is surgery fit only for satyrs; and yet the practical outcome of much of the prevalent treatment is as inevitably the ruin of the health of innocent women, as must be the result of following the coarse advice of this French surgeon.

Some who have paid but little attention to the diseases of women may consider the terms here employed to indicate the effect of the venereal poison upon the health of the woman unnecessarily strong. But it will be shown later on that the gonorrhœal virus may, and does frequently, cause chronic discharges, metritis and endometritis, salpingitis and pyosalpinx, ovaritis, peritonitis, derangements of menstruation, sterility, and a variety of complications and combinations of these diseased conditions; and, if this can be proved, any language fails to do justice to the facts. It may be also objected that such severe cases must be rare, and therefore the subject becomes comparatively unimportant. The frequency with which the more serious cases occur appears to vary in different countries—that is, as might be expected, according to the habits of the people. The apparent frequency also depends upon the method in which the facts of the history of each gynæcological case are investigated—that is to say, the nature of the cases is overlooked or detected according as the practitioners are ill or well informed on this special theme.

[1] "Le péril vénérien dans les familles." Par P. Diday, Paris, 1881.

That the gonorrhœal virus and puerperal septicæmia are the great factors in producing the more serious pelvic diseases cannot now be disputed against the weight of evidence; and there can be no doubt that a large number of the apparently puerperal septic cases are of gonorrhœal origin.

Cases Illustrating Phases and Combinations.

Without attempting, at present, to give any complete and precise description of a typical case of gonorrhœal disease in the female sex, including complications, as a guide to diagnosis and treatment, I shall mention in somewhat general terms a few fairly typical cases, with the view of bringing out in concrete form some of the various phases of the disease under consideration, keeping in mind only that, for the present, the disease has to be shown to be of common occurrence, and important apart from its frequency, and leaving definite conclusions as to diagnostic points and treatment to be developed in the sequel.

Case 1.—This patient when first seen was a married woman of 20. She had been married twelve months, and had not become pregnant. She complained of a pain chiefly felt in the left inguinal region, shooting across the hypogastrium, and making her feel sick. She has been worse for the last five or six weeks. Menstruation has so far been regular, but the last two periods have been scanty. Before marriage, menstruation was almost painless, and she was free from inter-menstrual discharge. Now the pain at the periods, coming on a day or two before and lasting until the flow ceases, is intense. It doubles her up, as she puts it; and she cannot sleep at night for the pain. Her ailment began three months after marriage. She had then some sort of acute abdominal disease, accompanied with severe hypogastric pain and scalding in micturition. This illness made her keep to bed for a fortnight. There is also mastalgia in the right side, intensified before the periods. Examination per vaginam shows that the uterus is in normal position and movable. Both ovaries are made out enlarged and adherent, and very sensitive to touch. These notes, taken twelve months ago, indicate the patient's condition then; she is now no better. She has been an in-patient of a hospital for women, and has been subjected to various measures of treat-

ment, with only temporary benefit. She is now a dysmenorrhœal invalid, and in all probability permanently sterile. Here then is a young, robust girl, whose health is deteriorated, perhaps entirely ruined, by marriage. What is the essential element in the causation of this result? I have not been able to detect the gonococcus, but the husband confesses to having contracted gonorrhœa within a year before his marriage, although he considered himself well when the marriage took place. Note the change in the type of menstruation in this case, often one of the most striking features in creeping gonorrhœa.

Case 2.—The next patient was, at the time of her marriage, three years ago, a robust healthy woman of 22, without any record of illness since childhood. A few months after marriage she began to suffer from vaginal discharge, with frequent and painful micturition. Menstruation, which used to be regular, normal in amount, and painless, became painful and profuse, ultimately developing into menorrhagia, for which medical treatment had to be sought. The first marked menorrhagic period was ushered in by an illness requiring rest in bed, the chief symptom of which was severe hypogastric pain. From this time the periods varied from one to three weeks, and were accompanied with severe pains, which continued during the whole time of the menstrual flow. An intermenstrual discharge is described as "running away" from her. The uterus, it appears, was dilated and curetted by the medical practitioner who first attended her, and the result was temporary relief from the hæmorrhage, but with no relief from pain at the menstrual periods. When she came under my care, a year and a half ago, I found that she had an enlarged uterus, evidently the result of metritis, and both her ovaries were enlarged and painful. She was submitted to treatment, varied in every way that promised to give relief, but with only temporary advantage. The third time she was admitted as an in-patient of the Manchester Southern hospital was after great suffering at a menstrual period, and when she had made up her mind to undergo any operation that might be considered necessary. The state of the ovaries was worse than ever, and accordingly, with the consent of all concerned, the ovaries and tubes were removed. That is six months ago. The tubes were somewhat dilated, and the outer extremities were incorporated with the enlarged and cystic ovaries. The

patient recovered without any bad symptom, and is now relieved of her sufferings, and she has regained to a large extent her healthy appearance.

There can be no doubt, I think, that the direct cause of all this injury to the woman's health was due to gonorrhœal infection: The husband had the disorder the year before he married, and though his statements have varied, he admits to having seen traces of the disease within six months of his marriage. He was and is addicted to drink, and, that being the case, it is easy to understand how the diseased process would be continued indefinitely in the latent form, and be ultimately stimulated by frequent sexual intercourse into such active development as to make it readily contagious.

Case 3.—In this case we shall see how the diseased process may continue indefinitely, while the woman is living under comparatively favorable circumstances, producing symptoms which, under other conditions, might call for operative treatment. The patient is 29 years of age, and has been married the second time five years. She came first under my care eight years ago, when her first husband was living. At present the form her ailment assumes is enlargement of the uterus, with retroversion and a tendency to prolapse. On exertion, the dragging of the uterus, when not supported, produces nausea and vomiting, which may come on quite suddenly during any kind of active exercise. The left ovary is enlarged and tender, and bands can be made out behind the broad ligament, which are the result of inflammatory adhesions. Near the vaginal orifice there are tender areas, which make it almost impossible for the patient to wear a Hodge's pessary, and yet a padded Hodge is the instrument which gives most relief to the other symptoms. This difficulty seems to be due to a chronic inflammation of the glands of Bartholini. The patient has been so far sterile since her second marriage; she menstruates regularly, but with severe pain, and scanty menstrual discharge. There is a considerable, though not profuse, leucorrhœa. Now, if a physician were being consulted by this patient for the first time, in her present condition, he would probably find it impossible to make out for certain the state of parts or the cause of the disease. It would be possible to elicit the history of a very severe puerperal illness over seven years ago; that illness was of gonor-

rhœal origin. I attended the patient during her pregnancy, while she was suffering from an acute attack of gonorrhœa, conveyed to her by her husband, in whom it was clearly of post-nuptial origin. She was only apparently cured by the end of pregnancy. She was delivered of a healthy child, but she was seriously ill for months. The severer symptoms came on nearly a month after the birth of the child, and arose from inflammation, extending to the pelvic peritoneum and including the ovaries. There followed pelvic abscess, and all the usual train of hectic and emaciation, with adhesions and fixation of the uterus. She made a very slow recovery, and was unfit for any exertion for many months. I have a continuous history of her ailments since then, because I have seen her at intervals during these seven years, and there can be no doubt but that all her troubles began with, and are the direct result of, the gonorrhœal infection during her first and only pregnancy. Since her second marriage this patient's ailment has been "latent." Her husband has never suffered from any sort of irritation of the glands or urethra, hence it may be confidently asserted that the wife's leucorrhœa has been entirely non-specific in its effects, although specific in origin.

Case 4.—M. N., æt. 22, single, strong, healthy-looking woman, complains of a pain in the left inguinal region, and in the thigh. Menstruation is irregular and profuse, sometimes lasting three weeks, and producing extreme weakness. There is intense dysmenorrhœa, the pain continuing during the first two or three days of the period. Much inter-menstrual discharge. On examination per vaginam, the uterus is found to be enlarged and fixed, with patulous os; there is a large, hard, not sensitive mass behind the uterus, with the usual accompanying hardness of the tissues round the left side of the pelvis. This patient had an illegitimate child twelve months ago, and she has never been well since. In the latter half of her pregnancy she suffered from swelling of the nymphæ and scalding in micturition, and had an extremely profuse mattery discharge. She is convinced it was a venereal disease that she had contracted, although she does not assign the reasons for this belief. The child began to have an inflammation in one eye, with mattery discharge, two days after its birth, and this continued for about a month, although the child was under treatment.

This is a common type of hospital case, occurring among women of the same class, both married and single. Repeated examinations of the discharge for the gonococcus gave no result, but the history permits of a confident diagnosis.

Case 5.—M. E. M., æt. 24, married six years, and has had four children. Last confinement six weeks ago. Has always had good recoveries until this time. Was confined to bed for three weeks, with pelvic pain after her confinement, and has continued to suffer from the pain to some extent since she began to go about. She has been troubled with a profuse yellow discharge since the lochia ceased. On examination, the uterus is found to be enlarged, with open os (sub-involution), and the left ovary is much enlarged and very tender to touch. Discharge from os, yellow, mattery, profuse. For the last two months of her pregnancy she had a slight discharge, which caused some irritation about the vulva, and a slight discomfort in passing water. She volunteered a statement which left no doubt that her husband was under treatment for a venereal disease contracted during the wife's last pregnancy. The child was under treatment as an out-patient of the Southern Hospital for *ophthalmia neonatorum*. Examination of the uterine discharge in this case, the matter being taken from the os uteri for the purpose, showed the presence of a micro-organism, having all the characteristic appearances of the gonococcus.

Case 6.—This patient was a rather scrofulous girl, of the domestic servant class, aged 19, who, when first seen, had been suffering for about six months from an ailment which was ascertained to be gonorrhœal in its origin. She had the usual hypertrophied uterus, with great enlargement and pain of the ovaries; the condition of the Fallopian tubes could not be differentiated. Medical non-manipulative treatment and rest produced much improvement in the course of six weeks, but even then the patient could not walk erect. After other six weeks' treatment by medicated vaginal tampons, without further improvement, I resolved to make a careful exploration of the pelvis with the help of an anæsthetic, and then decide on the question of operation. The careful examination was made, a sound was used, which had been thoroughly disinfected—which was, in fact, lifted out of a warm antiseptic solution in order to be introduced—and the result of the ex-

amination was a decision to operate if a short trial of the then universally favorite hot douche failed to give relief. The hot douche was used for the first time the same day, in the hope of relieving the discomfort caused by the examination, and next day the temperature began to rise. This was one of my early cases of the kind, and I temporised in the hope of giving relief by sedatives; but the after course was continuously downward. There was pelvic peritonitis with fixation of the uterus, and intense pain on touch. She never menstruated again. Ultimately pelvic abscesses formed, one bursting into the bowel and another into the bladder, and continued for months to refill and discharge alternately. The patient slowly emaciated, and ultimately died of exhaustion.

My belief with regard to what happened in this case, in the light of later experience, is this: The examination by the sound produced a congestion by its stimulating effect, which, assisted by the hot douche, stirred up into more active development the quiescent gonococci, resulting in a further spread of the inflammatory process, probably producing pyo-salpinx, or abscess of the ovary, and other abscesses. It is just possible that the sound may have introduced some pathogenic organism, which brought on a "mixed infection," or the tube may have been stimulated into discharging some of its contents into the pelvic cavity. The one thing certain about the case, whatever it may have been towards the end, was that it was gonorrhœal in its origin. If the ovaries and tubes had been removed when the temperature began to rise, the result might have been very different.

Case 7.—Another domestic servant, in whose case the only ascertainable cause for the lighting up of a fresh attack of ovaritis was passing the sound in examination. She confessed to having become affected with a venereal disease, with ordinary symptoms of a mild gonorrhœa, twelve months before. Since then her menstrual periods had become painful, and so profuse that her mistress suspected an abortion at the time I was first asked to see the patient. The girl was so reduced in strength by reason of her losses of blood, and pain from enlarged and tender ovaries, that she was unfit for work. She was admitted, at the request of her mistress, into the Southern Hospital. In the course of examination, a thoroughly disinfected sound was employed, and in 24 hours there was a dis-

tinct rise of temperature with unusual pain in the pelvis. The left ovary became more tender and larger, but in a few days it could not be defined because of a hard exudation in the left side of the pelvis. There was high temperature, with the usual red, dry tongue, but there was never any hectic. The temperature fell in ten days from the first onset of pyrexia, and the exudation could be pressed upon without giving rise to much complaint. All seemed to be going on well for about three days, when the temperature began to rise again, and the right side of the pelvis developed the same train of phenomena as the left. No abscess ever formed, and the patient ultimately recovered after an illness of two months' duration. When last seen her menorrhagia was cured, for menstruation had become scanty, but the dysmenorrhœa continued; she was still unfit for prolonged exertion of any kind.

Case 8.—Mrs. B., æt. 29, married seven years, had one miscarriage in the first year of married life, no pregnancy since. She came under my care two years ago, and was under treatment over twelve months without deriving any benefit. She had been always strong and healthy before she was married, and her husband is a well-developed, healthy man. On his side there is the history of gonorrhœa contracted about two years before marriage, but there is no evidence of a gleet continuing after the first apparent cure, and there are no habits of dissipation to make such a continuance or recurrence probable. There is no clear evidence of the conveyance of the disorder to the wife, all her early symptoms being possibly attributable to pregnancy. She aborted at four months without apparent cause, and suffered for a long time from some form of puerperal illness, accompanied with pain in the abdomen. No abscess appears to have formed. From this time menstruation became painful and profuse, and at the time she first came under my care she was entirely laid aside during her periods, suffering what was described as an agony of pain. She appears either to have had at these times short faints or some sort of slight epileptic seizures. She was tolerably well in the intervals. The ovaries were enlarged and painful, and there were some obscure points in the palpation, suggesting adhesions. Dilatation of the uterus before a period gave no relief to speak of. The final resort was oöphorectomy. Both the tubes were closed and adherent at the outer ends.

the right being greatly distended with turbid serum. The ovaries contained blood-cysts, and were adherent. The omentum had become attached to the extremity of the right Fallopian tube. Tubes and ovaries were completely removed. The operation took place nearly twelve months ago. The patient made a perfect recovery. She is now well, except for some nervous symptoms characteristic of the menopause.

This case, taken by itself, would prove nothing with regard to gonorrhœal infection. It requires the experience of many other cases more or less closely resembling it to bring out the fact that it is a very good typical case, and that we are justified in attaching what might otherwise seem undue importance to the points which make for proof of its gonorrhœal origin.

Case 9.—A lady, now 30 years of age, was married twelve years ago, and during the first year of wedlock contracted gonorrhœa from her husband. She had a miscarriage at seven months, about a year after marriage, and since then she has been a wreck. At present she suffers from enlargement of the uterus, which becomes completely anteverted at times on exertion, making even a moderate amount of walking impossible. Her ovaries are enlarged, especially the right, and they become very painful at the menstrual periods. Menstruation is scanty, and very painful. There is now hardly any leucorrhœa. The anteversion of the uterus causes much bladder distress at times. She is anæmic and thin, the reverse of what appears to have been her condition before marriage. There is in this case the history of a long serious puerperal illness, necessitating constant medical treatment for over twelve months. The patient has been under treatment for relapses at short intervals almost continuously since recovery from the first serious attack. She has never become pregnant again. She appears to have worn all manner of pessaries, and to have tried internal and external applications of every kind. She has had the uterus dilated once, resulting in a severe illness of some kind; and she used to have several days of suffering every time the sound was passed by any one of the numerous specialists whom she has consulted in the course of years. Among other therapeutic measures that have been tried has been median incision of the cervix uteri, the only remaining objective evidence of which seems to be a small notch on the posterior lip of the os. What the anatomical

condition is at present and how much of the deviation from the normal is to be ascribed to the original gonorrhœa, and how much to treatment, nobody could now profess to decide. Twelve months ago she consulted, at my suggestion, a celebrated London gynæcologist, who wrote to me: "She seems to me to have very little the matter," and went on to say that, in his opinion, she was suffering more from treatment than anything else, and he had advised her to give it all up, "to walk and dance and enjoy life." She was not satisfied with the advice given her by this physician, because she believed herself too ill to attempt to follow it, but she took his prescription to a chemist to be dispensed. The dispenser entered into conversation with her, and at his suggestion she went the same day to another specialist in the neighborhood whose name she had never heard of till then. This young gentleman wrote to me that he had diagnosed double pyo-salpinx, and had recommended operation. He went on to say: "If you do not care to undertake the operation, I would be *very pleased* to do it. I have been very fortunate with my cases of abdominal section, and *I look upon this as a very favorable case.*" I am responsible for the italics. Out of respect for the feelings of earnest and upright gynæcologists, I shall quote no more of this letter, but I must strenuously protest against any one professing gynæcology, whatever his excuse for ignorance, calling a case with a history of ten or twelve years of complications "a very favorable case" for operation. Favorable it could not possibly be, regarding either the immediate consequences of the operation or the remote results. Such cases are always difficult and dangerous because of the firmness and extent of organized adhesions; and they are disappointing in their later results, because the reorganization of the innervation of the parts is either very slow in following a radical operation, or it remains incomplete. Palliation, not cure, is the best that can reasonably be expected. Enough has been said to call attention, in passing, to these extremes of treatment for some of the complications arising from gonorrhœal infection, and to call up in imagination the effects upon the patient of such advice. In the case under consideration the patient, wisely, I think, has adopted as much as she could of the advice "to give it all up," and is certainly no worse, probably a little better, than she was last year.

Case 10.—Two years ago I had occasion to open a mammary abscess in a hospital patient, and I took some of the matter to the Pathological Laboratory at Owens College with the object of trying some cultivation experiments, which I had the opportunity of making under Professor Dreschfeld's friendly instruction and guidance. The pus was full of micro-organisms, some of which looked like gonococci. Tube cultivations produced a development like that obtained by Bumm from the gonococcus. No pure cultivation was carried out with this specimen. When the patient was next seen she was asked about her symptoms during pregnancy, and it then came out that she must have been infected with gonorrhœa while pregnant. The infant at the breast was suffering from *ophthalmia neonatorum*, and was also an out-patient of the hospital. The patient had so far no symptoms suggesting the existence of any pelvic complication. Her only ailment was the mammary abscess, which must have been produced by the extension of the inflammation along the milk ducts, and that inflammation must have originated in the implantation on the nipple of colonies of gonococci from the child's eyes. To go back a step further, the purulent discharge from the child's eyes originated in infection from the genital tract of the mother. The state of matters here described may have been a result of "mixed infection;" but without going into the discussion of that subject, I may claim, provisionally, this case as also an illustration of the consequences of gonorrhœa.

Cases might be multiplied indefinitely, but sufficient have perhaps been given for the present object, which is to convey a general impression of the importance and the frequency of occurrence of this class of disorders. It may seem strange to some to whom such observations are the mere commonplaces of practice, that so much is said about the importance of these disorders as a group of diseased conditions. But there can be no doubt that the subject is, as a rule, treated too lightly. It will be seen that a point common to all the cases cited is the absence of treatment in the early stages of the disease. The only apparent exception is the case which was under my care while in the acute stage; but even in this case the disease was thoroughly established before treatment was begun, and, besides, the treatment was of the ordinary inefficient routine sort which was in vogue eight years ago. How little success

attended it has been made manifest. As a rule, the disorder in women excites so little attention that the doctor is called in only to deal with complications when they arise.

The reasons for this are probably the absence in most cases of severe urinary troubles; the want of an evil conscience, which is usually present with the man; the comparative difficulty with which women can minutely inspect their pudenda when slight discomfort begins, and their natural shyness about submitting to the inspection of other eyes; and the comparative frequency with which some plausible reason for a discharge or discomfort can be assigned; it is, for example, the effects of intercourse soon after marriage, a derangement of menstruation from some supposed "cold," or some one of the disorders of early pregnancy. No doubt one active influence in preventing the detection of gonorrhœa in the woman, while it is yet in the curable stage, is the conviction on the part of the husband that the thing is of no importance if the wife can be kept in ignorance of its nature. Matters will assume a very different aspect when all concerned awaken to the importance of prevention, and the difficulty of cure when the disease has reached the stage of complications. It is necessary to guard against exaggeration, for there is a danger that in rousing from long ignorance and neglect of the subject, the professional mind may sway to the other extreme, and, amidst the phenomena of disease obscure in their nature and as yet inexplicable, be tempted to accept gonorrhœal infection as an easy and sufficient explanation of morbid processes with which it has no kind of causal relation. Still, as yet, the actual facts with regard to opinion are all the other way, and the danger which exists is not too strongly stated by a recent writer on the subject, who says[1]:—"The danger of gonorrhœa in the woman lies especially in this fact, that the infection from the urethra or vulva, vagina or cervix, may extend over the mucous membrane of the uterus, and thence further on to the tubes, the ovaries, and peritoneum, where it may give rise to a series of the gravest abdominal ailments. These may end fatally in acute peritonitis, resulting from the escape of pus from the tubes into the peritoneal cavity, or from the bursting of an abscess of the ovary, or of a pyo-salpinx; or they may give

[1] Dr. Fritz Levy (Copenhagen): "Om den 'latente' Gonorre hos Kvinden." *Hospitals Tidende*, Nos. 1, 2 and 3, 1887.

rise to a condition of chronic peritonitis with adhesions of the uterus, tubes, and ovaries to the adjacent organs, or to recurrent attacks of pelvic peritonitis with the ultimate development of a 'gonorrhœal cachexia,' and general breakdown of the health."

Frequency of Occurrence of Gonorrhœal Affections.

I have not seen any statistics worth quoting which could guide us to a definite conclusion as to the frequency with which gonorrhœa is to be met with in men and women in this country. Every medical practitioner in the large centres of population knows that it is one of the commonest ailments among men, but with regard to women the case is different. The disease, as it occurs in the female sex, varies so much in its features, that from the signs and symptoms alone it is usually looked upon as impossible of diagnosis. As the cases are not definitely diagnosed, there appears to be a general belief that the disorder is not nearly so common among women outside the classes of professed or clandestine prostitution as it is among men. We must, therefore, for the present, rest satisfied with little more than looking at the views of some foreign authorities, keeping in mind that most of the facts are of foreign origin, when we come to draw conclusions from them.

Noeggerath,[1] whose small work on "Latent Gonorrhœa in the Female Sex" marks the beginning of a new era in our clinical knowledge of the disease, says: "I do not know what the state of matters is in other cities; I did not know how we stood in New York until I questioned the husband of every woman who came under treatment. And I believe we may apply here the dictum of Ricord that in every 1,000 men, 800 have had gonorrhœa." In another place he says: "I believe I do not go beyond the mark when I assert that gonorrhœa in 90 per cent. of the cases remains uncured. Of every hundred women who have married men formerly affected with gonorrhœa, scarcely ten remain healthy, the others suffer from some of the ailments which it is the object of my essay to describe." Coming more into detail with regard to these affections, he says that his experience in New York, which he supposes to

[1] "Die latente Gonorrhœ in weiblichen Geschlecht." Bonn, 1872.

be a type of all the cities of the first rank, leads him to conclude that "after catarrh, chronic perimetritis is the most common ailment of the female sex."

Alfred Fournier, who writes the article "Blennorrhagie," in the *Nouveau Dictionnaire de Médecine*, 1866, says: "Blennorrhagia is perhaps the most common of all diseases. In the great centres of population, in the cities, where the people are facile in their habits and fond of pleasure, there are few men who escape it, and there are many who have had it again and again." In another place he says: "La blennorrhée est vulgairement connue sous les noms de *goutte militaire*, de *goutte matinale*, de *suintement habituel* ou *chronique*. Elle est d'une excessive fréquence, et cela à tous les âges, dans toutes les classes de la société."

Some German gynæcologists have noted the frequency with which the diseases of gonorrhœal origin occur in their practice, and the results strongly support the once much derided statements of Nœggerath.

E. Schwarz,[1] of Halle, in a lecture published last year, says that in 617 cases, carefully observed since the end of 1885, there were 112 which excited the suspicion of previous gonorrhœal infection, and in which the patients' statements and the still existing symptoms made the diagnosis more or less probable. Of these 112 there were 33=5.3 per cent. who proved to be the subjects of acute gonorrhœa, and of that number 19 were either unmarried or widows. In the whole of these cases, diagnosed by appearances and symptoms alone, the diagnosis was further demonstrated by the presence of the gonococcus. Of the remaining 79 cases the gonococcus was found in its characteristic groups in 44 cases, although in some it had to be searched for several times. Thus gonorrhœa was proved to be present in 77 out of 617 cases, that is, in 12.4 per cent. Schwarz is of opinion that many of the remaining 35 cases had been infected at some time or other, and that the gonococcus would have been found if examination had been made at the most favorable times (Prädilektionszeiten), shortly before or after menstruation, during pregnancy, or in the puerperium. Several of them suffered from perimetritic affections with fixation and dislocation of the uterus, purulent

[1] "Die gonorrhoische Infektion beim Weibe."—*Sammlung klinischer Vorträge*. Leipzig, 1886.

endometritis, or showed other suspicious signs, and with several there was a history of purulent ophthalmia in their new-born infants.

Sänger,[1] of Leipsic, who is perhaps the principal champion in Germany of views approaching to those of Noeggerath, gave the latest results of his observations in a paper read before the German Gynæcological Society at Munich last year. He does not consider that the diagnosis of gonorrhœa is established except by the clear statements of the man or woman, by the occurrence of ophthalmia in the new-born children, or by the presence of affections of the urinary tract and the vulvar glands. The last especially he considers pathognomonic. Out of 1,930 gynæcological cases which came under his notice, in private and hospital practice, in the previous year, Sänger found 230 cases of gonorrhœal disease, equal to 12 per cent., or one-eighth of all the cases. More recently still, of 161 cases he had found 29, or 18 per cent., of gonorrhœal origin. In 389 cases of pregnant women, he found that 100 had a purulent discharge, 26 per cent., and 40 of the children ultimately born suffered from ophthalmia neonatorum.

O. Oppenheimer,[2] of Heidelberg, working upon the material of Professor Kehrer's Clinic, endeavored to establish the relative frequency of gonorrhœal infection in women, partly by direct examination of the vaginal discharges, and partly by the occurrence of ophthalmia neonatorum. In 108 pregnant women, he found 30 in whose vaginal secretion the specific diplococcus was undoubtedly present; that is, in 27.7 per cent. Ophthalmia neonatorum occurred in from 12 to 13 per cent. of the cases.

Lomer,[3] of Berlin, examined some of the patients of Schröder's Clinic, just as they came, without any selection on the ground of previously existing catarrh of the uterus, and he found in nine out of 32 lying-in women the characteristic diplococcus enclosed in pus cells, that is, in 28 per cent. The cases in which diplococci in colonies were observed, leading to the suspicion

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[1] "Ueber die Beziehungen der gonorrhoischen Infektion zu Puerperalerkrankungen."— *Verhandlung der deutschen Gesellschaft für Gynäkologie*, Leipzig, 1886.

[2] "Untersuchungen über den Gonococcus (Neisser)."—*Archiv für Gynäkologie*, Bd. XXV., Hft. 1.

[3] *Deutsche med. Wochenschrift*, No. 43, 1885.

of gonorrhœal infection, amounted to 56 per cent. of all examined.

The frequency of the occurrence of the disorder varies so much in different localities that it is, and perhaps always will be, impossible to formulate any statement which will be of general application even to cities. A curious example of this diversity is quoted by Noeggerath in a recent paper.[1] He refers to Winckel's statement that when he was at Dresden he was never able to demonstrate a single fatal case of acute gonorrhœal salpingitis in 400 female bodies examined, whereas soon after his transference to Munich he met with many cases of acute gonorrhœal salpingitis and peritonitis, and among them one fatal case. "In Dresden in eleven years not a single fatal case, in Munich in three years and three quarters three cases."

With regard to the material on which my experience in Manchester has been acquired, I am not prepared to hazard any definite statistical statement at present. In private practice the occurrence of some of the gonorrhœal diseases of women, now that they are diagnosed as a rule, is common enough; but they are by no means the most ordinary ailments which one is called upon to treat. In the current list of patients the disease is never without two or three unequivocal witnesses to its existence. In hospital practice, among the class of women who are not very particular in their notions of personal cleanliness, it is a very common disease. Married men of the operative class, when out of work, appear to contract some form of venereal disease in amazingly large proportion, and to take little or no precaution to save their wives from the misery resulting from the contagion. It is a social question which it would be hard to settle, whether the poorer married women of the working class suffer most from the effects, including sterility, produced by the venereal diseases conveyed to them by dissolute husbands, or from the constantly recurring child-bearing and lactation, which fill up the burdensome prime of life for the healthy wives of the more virtuous or fortunate. Among the purely gynæcological cases, as they occur in my hospital practice, the proportion of cases of gonorrhœal origin is about 1 in 15. Of the cases of pelvic

[1] "Ueber latente und chronische Gonorrhœ beim weiblichen Geschlecht."—*Deutsche med. Wochenschrift*, Dec. 8, 1887.

peritonitis, in any of its forms or phases, gonorrhœa is the cause in an overwhelming proportion, the fraction of the whole next in amount to the gonorrhœal being that made up by neglected cases of abortion.

From the contemplation of such facts as these it is a relief to turn to the other extreme. Milton,[1] speaking of a small town in Cumberland, says: "Having had the opportunity of tracing this disease for many years back, in what was then a very small town in the North of England, where gonorrhœa is now rather firmly established owing to the growth of the place, I was able, by means of the books of a successive line of surgeons, kept for a long time, to make out pretty certainly that in their practice it had, till about forty years ago, only been very rarely seen and sometimes not heard of for years together. All the inquiry I could make tended to fortify this opinion: the general experience seemed to be that gonorrhœa always died out soon after it was acquired." In another place he says: "During a four years' apprenticeship to a surgeon, who, though living in a very small town, had one of the largest practices in Cumberland, I saw but very few cases of gonorrhœa, certainly not a dozen, though every instance of such a disease must have come to my knowledge. Of these I know that some were caught from sources foreign to the place."

With regard to the prevalence of these disorders, we can readily infer that between their frequency of occurrence in the cosmopolitan cities and dense centres of population, and their rarity in sparsely populated rural districts, there may be every grade of proportional frequency. Consequently, if the profession as a whole is to arrive at a just comprehension of the facts, the conclusions reached by each individual as the result of his experience must be modified and corrected by the experience of those practising under every degree of difference in circumstances. If this fact were kept in mind, we should find the history of the discussion of the subject under consideration less embellished with sneers and triumphant rejoinders than it is. For example, we find Milton discussing Noeggerath's conclusions without having acquired any clearer notion of them than could be obtained second-hand from a review, and with mildly sarcastic superiority brushing them aside. "It does

[1] "On the Pathology and Treatment of Gonorrhœa." By J. L. Milton, 5th Edition, London, 1883.

not seem to have struck Dr. Noeggerath," he says, "that, had his facts been correct, *gonorrhœa would have long ago depopulated every country into which it penetrated.*"[1] It will be seen, however, on reference to Noeggerath's words, which I have been careful to give literally, that he explicitly states that his allegations do not apply to the state of any community in respect of this matter except New York, with which alone he is familiar. If we had only our crowded world-cities to trust to for the continuance of the race, the world would soon be depopulated, or worse, from more potent causes than gonorrhœa. If the statements on either side of the question of frequency of occurrence are a little strong, the conclusion of the whole matter only amounts to this: that for the physician in the large city, gonorrhœa is a disease of primary, practical importance; for his contemporary in the rural district it is more a matter of speculative scientific interest.

[1] *Op. cit.*, p. 53.

CHAPTER II.

HISTORICAL RETROSPECT OF VIEWS ON THE PATHOLOGY OF GONORRHŒA IN WOMEN.

In order to obtain a clear view of our present position with regard to the pathology of gonorrhœa and the effects of the disorder, it seems to me expedient to give a short historical retrospect of the path by which our present position has been reached. We shall then be better able, without the need for repetitions, definitely and concisely to consider the special phases of the disease with which we are at present concerned; to examine the phenomena of the affection as it occurs in the female sex, the consequences which infection may entail, and the prophylaxis and treatment, and any medico-legal, moral, and social questions which may naturally arise out of the whole case.

For our present purpose the past may most conveniently be divided into three periods—(1) Before Noeggerath's treatise appeared; (2) Noeggerath's work and immediate influence; (3) Neisser's discovery.

Before Noeggerath.

(1) The first period takes us back, according to the ordinary fashion in medical histories, to the time of Hippocrates. For practical purposes we may rest satisfied with looking to the more modern epoch when Ricord flourished. Ricord's views as to the non-specific nature of gonorrhœa dominated the profession in his time, and do to a large extent still prevail. There was always a strong minority who held the opinion that the disease was specific, but they were in the position of mere agnostics, who could not accept the "frivolous anecdotes" on which their opponents seemed to ground their faith, rather than a school of scientific opinion founded on research and observation. The successive failures of the specificists to

demonstrate the presence of an organic virus in the form of a micro-organism was claimed as still stronger support of the antagonistic views. Several investigators, each in turn, claimed to have discovered the specific organism. Donné's *trichomonas vaginalis*, for example, held the field for a considerable time as the organism whose presence produced the phenomena of vaginitis; but the anticipations of its discoverer and those who accepted his opinions were doomed to disappointment. But the existence of a micro-organism to carry the disorder was not a necessary part of the belief of those who held to the specific nature of gonorrhœa. The position taken up by Sigmund and Auspitz of Vienna, Durkee in America, and perhaps also by Milton and other authorities in this country, was that gonorrhœa can develop only from gonorrhœa, and some of these certainly held to the view that the specific virus resided in pus as compared with any other form of secretion. On this opinion depended some important practical conclusions, and we shall see that with regard to the precautions to be taken to prevent the spread of the contagion the believers in specificity were as faulty as the opposite camp.

Ricord, Fournier, and Diday were the chief authorities from whom orthodox writers, in this country and elsewhere, drew inspiration, and confidence in the correctness of their theoretic views.

Mr. Henry Lee, in the article in Holmes's "System of Surgery" already referred to, under "Causes of Blennorrhagia," mentions, in addition to the usual direct contagion, the action of irritating substances and constitutional causes. He then, in support of his position, quotes from Ricord a passage which I transcribe as well adapted to our present purpose:—"If we investigate with the greatest care the exciting causes of gonorrhœa—and I am now speaking of characteristic cases of the disease—we cannot help admitting that a gonorrhœal virus is absent in the majority of cases. Nothing is more common than to find women who have occasioned gonorrhœa unsurpassed in intensity and persistency, and attended by the most serious complications, and who are yet only affected with uterine catarrh, which is sometimes hardly purulent. In many cases, intercourse during the menstrual period appears to be the only cause of the disease; while in a large number we can discover nothing, unless, perhaps, errors in diet, fatigue, exces-

sive sexual intercourse, the use of certain drinks, as beer, or of certain articles of food, as asparagus. Hence the frequent belief of patients, which is very often correct, that they have contracted their gonorrhœa from a perfectly sound woman. I am most assuredly familiar with all the sources of error in such investigations, and I will presume to say that no one is more guarded than I am against the various forms of deceit which are strewn in the path of the observer; yet I confidently maintain the following proposition: *Gonorrhœa often arises from intercourse with women who themselves have not the disease.* Any one who studies gonorrhœa without preconceived notions, is forced to admit that it often originates from the same causes that give rise to inflammation of other mucous membranes."

When the masters in this peculiar field of science felt the need of strong language to bolster up such flabby opinions on causation as this passage implies, we need hardly feel surprise at any vagaries of the ordinary disciple. After reading a series of the stories by which the non-specific view is maintained, one hardly feels the absurdity of the suggestion made by a surgeon, mentioned by Milton, that a certain case of gonorrhœa might have originated from making water in the night air.

With regard to the phenomena of the disease in women, the predecessors of Noeggerath held the erroneous view that the vagina was the chief seat of pathological change. If the urethra and bladder were not involved, producing the characteristic symptoms, and if no coarse changes had occurred in the vagina, the surgeon was not in a position to decide with confidence whether or not he had to deal with a venereal disease. A discharge from the uterus was to him the product of a uterine catarrh, a condition quite separate and distinct from any venereal affection, and in only a very few severe cases had the observer confidence to allege any causal relation between the venereal virus and the uterine or pelvic disease. It followed from such loose notions as these with regard to the chief seat of the malady, its superficiality in an anatomical sense, and its non-specific nature, that the surgeon felt himself justified in pronouncing, from mere inspection, any suspected female clean or otherwise. It requires little imagination to grasp the vast social importance of this mis-

taken view of the pathology of so common a disorder; and that it was a mistaken view it is the chief object of this essay to emphasise, because all the rest depends upon it. If a concrete example of the social results of a pathological error be demanded, it should be remembered that the Contagious Diseases Acts, now repealed, were passed and administered in the United Kingdom, partly on the basis of this discredited pathology. Yet the medical profession is so indifferent to revising its opinions on this subject, and so confident in its old prepossessions, that it is probably not going beyond the mark to say that, if the re-enactment of these statutes depended upon a *plébiscite* of the qualified practitioners in this country, taken without further discussion, the laws would at once again come into force.

With regard to the disease, as affecting the male sex, the *crux* of the position was the belief that the pus cell was the pathological unit. The pus was the morbific agent, but inasmuch as any pus cell, whatever its origin, might be sufficient, the disease was not specific. The practical result of this belief was that men, just recovering from gonorrhœa, were assured that if only the remaining discharge was clear and glassy they might indulge in sexual intercourse without fear of conveying the contagion. With some it was a difficult question to decide when the discharge became sufficiently clear to be innocuous, and, for safety, many surgeons stuck to the rule that there must be an entire disappearance of the discharge before they could sanction sexual intercourse. "So long as *any discharge exists* sexual congress is unsafe,"[1] is a dictum containing the most advanced opinion of this school. This expresses by no means the general opinion and practice. "But not only does the medical world believe that a so-called cured gonorrhœa is actually cured, but they are even of opinion that a man who has a gleet (Nachtripper) may not infect his wife. It is usual at the present time with the best-informed practitioners (non-specialists) to sanction marriage in the cases of men who still continue to observe adhesion of the urethral orifice and staining of the linen, as *beaux restes* of a gonorrhœa. Even the highest authorities, as Professor A. Geigel, permit the cohabitation with his newly-married

[1] Mr. Henry Lee, in Holmes's "System of Surgery."

wife of a man, the subject of gleet, so soon as the urethral discharge appears perfectly clear."[1] Such was the state of practice and of doctrine with regard to gonorrhœa, when a specialist in diseases of women began to comprehend and explain the meaning of certain pathological conditions of the female sexual organs which he had long observed. The establishment of the relation of cause and effect between the neglected, apparently trifling and innocuous, chronic gleet in the male, and inflammation of the pelvic peritoneum in the female sex, is one of the most important and interesting chapters in modern gynæcology.

Noeggerath's Work and its Immediate Influence.

(2) The work which I am specially desirous of doing justice to, because of its originality and intrinsic merits, is that of Dr. Emil Noeggerath, a German physician, formerly practising in New York. His "grand idea" is expounded in a treatise, a mere "opuscule" in respect of physical proportions, published in German in 1872. The peculiar mode of publication has been a misfortune to English readers, and it has largely detracted from the influence which the book ought to have exercised. It has never been translated into English, and this fact seems to justify me in drawing largely upon the words of the original in support of the views which I am seeking to advocate. When it first began to dawn upon me in the course of gynæcological practice that many of the unexpected mishaps, and the whole course of many of the most intractable cases, were due to the gonorrhœal virus, I naturally turned to the literature in order to learn what was already known on the subject. Comparatively late in the search I had the opportunity of reading Noeggerath's monograph, which, until then, I had known only by hearsay. Like every other man I have hitherto met, I knew of Noeggerath as a German doctor who had actually published the outrageous doctrine that clap is an incurable disease, and as nothing more. It was, therefore, surprising to find, on perusal of the work, that only the undeniable exaggerations had been seized upon and noised abroad; the admirably clear expositions of the fruits of clinical work of the highest excellence, and the great idea

[1] Noeggerath, p. 2.

which inspired the whole and formed an advance on all that had hitherto been written on the subject, appeared to have fallen, for the most part, as seed on stony ground.

Noeggerath's work was largely clinical, and in this respect it contrasts with much that is to follow, which is mainly the work of pathologists and bacteriologists, engaged in research and observation without such close relation to the actual phenomena of disease. He, however, clearly enunciated the microbiotic nature of the disease, and indeed he almost believed, like some of his predecessors and contemporaries of the specific school, that he had discovered and succeeded in cultivating the special organism. "There is hitherto awanting," he says, "a so-called direct proof. If it were already proved in which form-elements the gonorrhœal contagion is exclusively bound up, if it were demonstrated that the pus corpuscles, and the pus corpuscles only, were the carriers of the contagion, then perhaps elements might be discovered in the secretions of the woman by careful microscopic examination which would throw light upon the origin of the affection.". . . "The whole meaning and importance of micrococci and of the fungi derived therefrom bear as yet so clearly the stamp of incompleteness, and are viewed with distrust by so many distinguished men of science, that I cannot expect any of my readers to attach very great importance to the presence of a fungus in forming their conclusions on the question. The subject must be further investigated by the mycologists in co-operation with one or other of the gynæcologists." Although it would be an exaggeration to call upon the reader to admire these sentences as a prophecy from the remote past, or as bearing the evidence of far-reaching scientific vision, still they show a very clear appreciation of the state of contemporary knowledge, and of the course that future research must take in order to be successful. It is evident that if Noeggerath had enjoyed the advantage of knowing Koch's methods of investigating the life-history of micro-organisms, that the missing link in the chain of evidence which he sought for would soon have been found, and the discovery of Neisser might have been anticipated by seven years at least.

Let us now examine Noeggerath's clinical work. He says that his object in publishing his observations is "to depict in their characteristic features a group of diseased conditions

peculiar to the female sex, and to prove that certain phenomena observed in the sexual organs, which have hitherto been looked upon and treated as distinct, possess a common basis from which, collectively and separately, they are derived." For this common basis he selected the name "latent gonorrhœa," because "it may be present for weeks, months, and even years, in the affected individual before it displays itself by any of its characteristic phenomena." In explaining further the nature of latent gonorrhœa, he says: "I have undertaken to show that the wife of every man, who at any time of his life before marriage has had gonorrhœa, with very few exceptions, becomes affected with latent gonorrhœa, which sooner or later shows its existence by some one of the forms of disease about to be described. The reason why this fact has not hitherto been brought under discussion in a radical fashion is grounded on several circumstances. In the first place, we physicians have hitherto believed that a gonorrhœa in a man, after it has once ceased to exhibit any signs of its existence, such as occasional moistening or adhesion of the urethral orifice, even itching, or discomfort in micturition, is actually cured. Such is, however, in the great majority of cases, not the fact, and I believe I am not going beyond the mark when I say that 90 per cent. of cases of gonorrhœa remain uncured. Of 100 women who have become the wives of men who have formerly been affected with gonorrhœa, scarcely 10 remain healthy; the rest suffer from one of the ailments which it is the task of this treatise to describe."

In order to prove his theses, Noeggerath gives the notes of fifty selected cases, which are so arranged as to illustrate the various heads under which he discusses his subject. These clinical groups, under which he classifies his observations, are: (1) Acute perimetritis; (2) recurrent perimetritis; (3) chronic perimetritis; and (4) ovaritis. All the four varieties of diseased processes are complicated with catarrh of distinct portions of the mucous membrane of the sexual organs, and this catarrh, in a few cases, is found to be the only sign of disease. Although this classification may now be considered obsolete, if even it could be considered originally established by the author's own material, it did good service by calling attention to the extreme frequency of perimetritis as a consequence of the gonorrhœal infection. It may be a question whether it is

possible clinically to distinguish between the three varieties of perimetritis, or whether every attack of perimetritis is not necessarily always more or less acute, ultimately becoming more or less gradually chronic, and liable at any time, under favoring conditions to become recurrent. In any case we may accept that which is implied in the classification as something which clinical experience since Noeggerath's time tends more and more to establish, viz., that there is always catarrh, and in the great majority of cases perimetritis. "Inflammation of the female sexual organs, as it occurs in consequence of latent gonorrhœa, whether acute or chronic in its course, is in every case periuterine—that is to say, it affects the serous covering of the pelvis, and of the organs contained in it." In 100 cases of this disease, occurring in the author's practice, not one can be recalled to memory in which the morbid process began in the parametrium. After a criticism of the views of Matthews Duncan and the statistics of Bernutz, he concludes that, provisionally setting aside the cases which are said to have originated in the puerperal state and from menstruation, Bernutz also supports the opinion that gonorrhœa and syphilis are the most prominent causes of perimetritis. "But not only does the florid, acute gonorrhœa supply the principal contingent of this class of disease, but the so-called latent gonorrhœa is quite as important as the acute form. And I may add (1) that a woman who, at any time of her life, has had an acute gonorrhœa, has to expect some time, it may be after months or years, one or more attacks of acute, sub-acute, or chronic perimetritis; (2) that the wife of a man who, at any time of his life, before or during wedlock, has suffered from gonorrhœa is, with regard to an attack of perimetritis, in the same position as if she herself had had an acute gonorrhœa

"Under these two groups of circumstances a woman must expect at some time or other in her life to become the subject of a pelvic inflammation, sometimes ending only at death. If it comes to an acute manifestation of the affection, the case usually takes something like the following course:

"The man, either already a dweller in a large city, or in his capacity as traveller, student, etc., has become initiated into the mysteries of modern civilisation by contracting gonorrhœa. This disease, although it may have apparently disappeared without leaving a trace behind it, makes him for many

a day capable of conveying the contagion. The young, hitherto healthy, wife begins to complain a few weeks after marriage; attention to her domestic duties becomes a burden to her, and pedestrian exercise which could formerly be taken without the least effort now gives rise to signs of fatigue; menstruation becomes more profuse than formerly, and there are pelvic pains during the first days of the periods; a little vaginal discharge follows each period, and this, gradually increasing, ultimately continues without intermission until the next menstrual period begins. After a few months, really severe pains come on either in the left or the right half of the pelvis, and the sufferer is ultimately compelled, on account of feverishness and unbearable burning in the abdomen, with increased discharge, to take to bed and send for medical help. According to the severity of the attack she remains confined to her bed for weeks or perhaps for many months, with exhausted strength, struggling for life, ultimately slowly recovering, but remaining sterile and invalid for the rest of her days.

"It not unfrequently happens that the woman who is married under such circumstances soon becomes pregnant, and during her pregnancy she suffers from pelvic pains which are supposed by herself and the doctor to be necessary drawbacks of her condition, and so she receives no particular attention. It sometimes happens that the symptoms become so urgent as to call for active treatment in order to prevent miscarriage. Labor ultimately comes on, and is followed by a severe endometritis with perimetritis, the former or the latter being the more prominent feature of the case. The development of this inflammation may begin either immediately after the birth, or, as is more frequently the case, it may come on eight to fourteen days, or even six to eight weeks after."

It is a peculiar fact that some women directly after marriage with a man who has formerly had gonorrhœa begin to exhibit symptoms of serious inflammation, whilst others may be years before they emerge from the latent period, and others again show such trifling departures from the normal condition that it is difficult to say whether they are affected or not. It may be set down as a law of this disease that "the earlier the first cohabitation occurs after the time when the gonorrhœa was pronounced to be cured, the shorter is the period of latency in the woman, and the acuter are the symptoms."

Space will not permit me to transcribe all Noeggerath's interesting cases, and it must suffice to select one from the first series.

Case II (Noeggerath's Case 5 [1]).—"Mrs. M., a native of Boston, had been, when I first saw her, married five years to an advocate in New York, who about one year before his marriage had undergone two months' treatment for gonorrhœa. The wife, who before marriage was a type of robust health and beauty, began soon after marriage to have ailments; she remained sterile, and suffered from pain at the beginning of her menstrual periods, and, what had never before occurred to her, began to have a slight fluor albus shortly before the periods. After a year she consulted Dr. Marion Sims, who performed on her his operation of incision of the cervix, with the object of curing the sterility. This proceeding was followed by such severe hæmorrhage as to necessitate tamponade of the vagina. On the following days pain began, and gradually increased to an enormous severity. The doctors in attendance found that the cause was an acute perimetritis. The patient was confined to bed for two to three months, and since that time she has never had a day's good health. She consulted one after the other the principal gynæcologists of New York and Boston; by one she was cauterised for ulcer of the cervix; another applied a large blister to the hypogastrium on account of chronic metritis; and a third made her wear an intra-uterine pessary for two months. A careful examination revealed the following facts: the uterus was anteverted and but slightly movable; the left ovary was small, hard, and firm, and fixed in the pelvis by adhesions; whilst the right ovary, lying deeper, seemed to be greatly swollen, rounded, and softened. Both ovaries were intensely painful to touch. The vagina was reddened, and bathed in a muco-purulent discharge, and there was catarrh of the glands of Bartholini. This lady had suffered inexpressibly during the last four years, not only at the menstrual periods, but during the intervals. The sleep was broken. . . . . I gave a very doubtful prognosis, and as soon as I saw that neither narcotics nor absorbent medicines produced the least effect upon her condition, I advised her to visit a German watering-place.

[1] *Op. cit.*, p. 18.

My advice was concurred in by a gynæcologist in Paris, and the patient on my strenuous recommendation spent two seasons at Kreuznach. On her return she felt in many respects better, but by no means completely restored to health." This patient ultimately left New York on account of symptoms of commencing tuberculosis, and the author could learn nothing of her subsequent history.

The chapter on "Recurrent Perimetritis" contains some passages which cannot fail to arrest the attention even of those familiar with the literature of the subject. The author has never seen a case of recurrent perimetritis in which he failed to prove the former existence of gonorrhœa either in the woman or in the man. He cannot understand how the phenomena of the disease are to be explained, except by the occasional emptying of the irritating contents of one or other Fallopian tube into the pelvic cavity, but as to the reason why this accident should occur in only a few women he cannot offer any suggestion. He thinks that any stimulus capable of producing sudden powerful contractions of the uterus and Fallopian tubes may produce in that way expulsion of the contents of the tubes into the pelvic cavity, and among these causes, which have been illustrated by cases of specific tubal catarrh in his own practice, he mentions: coitus after long absence of the husband, introduction of the uterine sound even in cautious and experienced hands, the application of bland intra-uterine medicaments, the wearing of intra-uterine pessaries, incision of the external or of the internal os, dilatation by sponge tents, and other manipulations. And such results he has observed only as the consequence of manipulations in women who were the subjects of latent gonorrhœa. "At least the presence of this affection explains, in by far the largest number of cases, the occurrence of the so-called 'accidents,' which, to the astonishment of the much-cutting uterine surgeon, sometimes come upon him like a thunderbolt from a cloudless sky. . . . I am far from saying that every fatal result of these minor operations is the result of perimetritis due to tubal catarrh, and I am persuaded that phlebitis and lymphangitis supply their contingent. This last, however, is the exception, the first the rule."

The notes of a case of recurrent perimetritis make, as a rule, a long story, and it would be tedious if I were to quote any of

Noeggerath's cases in full. We are concerned at present only with the relations of supposed gonorrhœal infection to the after-history, and the author's evidence in proof of such relations can be exemplified by extracts from a few typical cases.

His eighth case is that of Mrs. F., a well-developed and beautiful Englishwoman, who was married to a young merchant in 1861. The gentleman had been under treatment for a rather obstinate gonorrhœa by a friend of Noeggerath's, but for three months before his marriage not a trace of the disease was to be seen. He was assured that it was quite safe for him to get married, and he acted on the advice. All went well for about six weeks, and then the lady began to complain of a pain in the side, which at last increased to such a pitch that she had to take to bed. The husband's doctor was consulted, and diagnosed pelvic peritonitis, which he treated energetically. The patient was confined to bed for two months, and has been ailing ever since—1861 to 1872. All the symptoms are referable to the condition of the pelvic organs, which is given in detail. Then follows the history of ten years of bad health, varied with periods of more acute suffering.

The next case is that of a lady who was brought to New York in the beginning of 1872 to be under the author's care. When a bachelor the husband had suffered from gonorrhœa, which required many months for its cure; but it had disappeared for two years before marriage. In answer to the question whether every trace of it had disappeared, he admitted having noticed, after his marriage, an adhesion of the urethral orifice, and to have experienced occasional discomfort in micturition. Ten months after marriage the wife was confined of a healthy child, and since then (18 years) she has never become pregnant again. Soon after her confinement she began to complain of pain in the left side, and a sense of weakness in the pelvis. Then follows a history of wanderings in search of health from one European health-resort to another, and back to America. There were six distinct attacks of pelvic inflammation. Digital examination proved the existence of a mass of exudation in the pelvis, enlargement of the ovaries, and matting together of the pelvic organs generally. Noeggerath evidently despaired of doing any good, and recommended her to visit a Canadian watering-place.

These are fair examples of the half-dozen cases given as illustrations in this portion of the work. They have all these two points in common, that they are incurable ailments, entirely destroying the health and happiness of women who were healthy before marriage, and that they all show a history of gonorrhœa in the husband, which is brought out in a more or less convincing fashion as the cause of the wife's sufferings.

One more case may be quoted, chiefly for the sake of illustrating a point to which attention must be called later on, viz., the import of *neglected* gonorrhœa in men in relation to the gonorrhœal infection in women.

Case 12 (Noeggerath's Case 19).—"Mrs. V., an American lady, married six years before, as a healthy girl, to a man who suffered from a neglected gleet until shortly before marriage. The husband assured me that for two months before marriage he was quite well. Directly after the marriage the wife began to complain, had a leucorrhœal discharge, and suffered from pain in the right side, and sacralgia. Menstruation also became irregular and painful. She was treated by a series of doctors without any lasting benefit. On examination, I found a very sensitive 'succulent' uterus dislocated to the left, both ovaries very painful, especially the right, which was enlarged and fixed close to the uterus in an exudation mass. There were large ulcerated areas on the labia, and catarrh of the glands of Bartholini. After two months' treatment the patient had a slight attack of acute perimetritis." . . .

In the chapter on chronic ovaritis and catarrh, the author calls attention to the importance of inflammation of the glands of Bartholini as a sign of previously existing gonorrhœa. It has been usual to rely on the presence of an inflammation of the urethral mucous membrane as a diagnostic mark, but this is comparatively evanescent; the reddening of the orifices of the vulvo-vaginal glands, on the contrary, remains for years. "In the natural condition the openings of the ducts of both glands are seldom visible to the naked eye. When, however, you examine a woman who in former years has suffered from gonorrhœa, it is the rule that if you pull the labium minus away from the remains of the hymen, you see, between the upper and lower caruncula myrtiformis, a deep red point, covered with the glassy mucus. From this point, as a centre, there extends upwards and outwards a streak, which grad-

ually becomes paler, and ultimately fades into the color of the surrounding mucous membrane." These appearances are said to be characteristic of catarrh of the glands of Bartholini. That such an inflammation is caused by gonorrhœa, and that it is persistent, there can be no doubt, but whether it is characteristic of gonorrhœal inflammation alone, or may result from inflammatory conditions set up by other causes, yet remains to be settled by further clinical observation.

On the subject of sterility as a consequence of latent gonorrhœa, Noeggerath carries his conclusions further than the evidence produced seems to justify. He maintains that gonorrhœa is a common cause of sterility in the man, producing azoospermia, and he gives cases in proof. He is more convincing in dealing with the analogous effect on women, and he makes out a better case, though here also he leaves an impression of going beyond the record in the statement of opinions.

His treatment calls for little notice, not because of any deficiency in its merits, but because for our present purpose it is irrelevant. It is the treatment pursued by a judicious, scientific, and most patient physician, yet the most striking thing about it, perhaps, is its inefficacy. Noeggerath never hints at operative treatment, except to condemn it, but it is probable that few chapters have ever been written in more eloquent and telling support of surgical interference in this class of ailments than the portion of his short work which is devoted to treatment. Neither is this the place to deal with any conclusions which may suggest themselves from considering Noeggerath's work in the light of later experience, or to discuss wide-reaching questions which arise out of the subject and to which he himself explicitly calls attention. His more definite conclusions are perhaps best given in a nearly literal rendering of his own words:—

(1) "Gonorrhœa in the man, as well as in the woman, persists for the whole life-time, in spite of apparent cure.

(2) "There is a latent gonorrhœa in the man as well as in the woman.

(3) "Latent gonorrhœa in the man as well as in the woman, may evoke in a hitherto healthy individual either a latent gonorrhœa or the symptoms of an acute attack.

(4) "Latent gonorrhœa in the woman manifests itself in

course of time by perimetritis, acute, chronic, or recurring; or by ovaritis, or as a catarrh of some definite portions of the genital mucous membrane.

(5) "The wives of men who at any time of their lives have had gonorrhœa are, as a rule, sterile.

(6) "Such women, if they do become pregnant, either abort or bear only one child. Exceptionally three or four children are born.

(7) "From the discharge of a woman affected with latent gonorrhœa a fungus may be cultivated, which is exactly analogous to that obtained from the discharge of acute gonorrhœa in the man."

Much of this is now merely matter of historic interest; as the expression of opinion which first attracted serious attention to the subject, and led to the further observations which have brought about an entire revolution in the professional estimation of the importance of this class of disease.

Noeggerath has lived to greatly modify his first impressions. In the paper already referred to (p. 22) he states that he has given up his pessimistic stand-point, viz., that gonorrhœa is incurable, and that ninety per cent. of all married men who have had this disease infect their wives. He admits that if you ask ten men, eight or nine may say they have had gonorrhœa, yet it would be unjustifiable and arbitrary to assume that any disease of the organs of generation occurring at a later time in the wife is due to gonorrhœic infection.

When husbands deny that they have retained traces of gleet or a gonorrhœa until just before marriage, Noeggerath's rule is to thoroughly examine the urethra. Some of the worst cases of acute and recurring perimetritis which he has seen have occurred in the wives of husbands who had been dismissed as cured from gonorrhœa shortly before marriage. Of 24 patients suffering from acute and recurring perimetritis 12 were married to men who were cured one to three months before marriage, one man had been cured $5\frac{1}{2}$ months, another a year, six had been healthy two years before marriage, two married $2\frac{1}{2}$ years after stoppage of the gonorrhœa, one had had no symptoms of disease for 10 years, and one for 11 years. These are the opinions formed by 15 years' further experience. His views with regard to puerperal infection will be mentioned in the proper place.

Noeggerath's first work was more an influence than an extensive addition to the sum of knowledge; a fruitful idea, under whose inspiration other men saw in a fresh light the facts of daily experience, and could recognize in them the material suitable for building up the required superstructure of new knowledge. We can only look at the work of the most important contributors, those who by observation and research have added the largest amounts to our knowledge, or who have modified in some important respect the general views by the contribution of influential ideas.

The first fruits of Noeggerath's work in Britain appeared early, if the crop has not been extensive since. In 1873 Dr. Angus Macdonald[1] read a paper before the Obstetrical Society of Edinburgh, which contained a report of some striking cases in support of Noeggerath's position, and an expression of opinions which might almost be called prophetic. In the course of his remarks he says that Noeggerath "really seems to prove his positions well, strong and strange though they appear to be. I must confess, however, that I cannot help feeling convinced that he proves too much. . . . That, however, Dr. Noeggerath has got hold of a grand idea, and one which possesses a large amount of evidence in its favor, no one, I think, can deny who reads the recorded cases fairly." The author then proceeds to give the details of seven cases, in which gonorrhœal infection had given rise to more or less severe puerperal illness. The gonorrhœal puerperal fever was in one sad case fatal. The whole of Dr. Macdonald's cases go to disprove a point that Sänger has recently insisted upon, viz., the constantly late onset of the gonorrhœal form of puerperal fever as compared with the early appearance of symptoms in cases originating otherwise. That some gonorrhœal puerperal cases are late in developing their severer symptoms, there is little room for doubt, but the cause of variation in this respect is still in obscurity. For the sake of calling attention to this point, which is obviously important, and interesting inasmuch as it is still unexplained, it may be worth while to insert here Dr. Macdonald's first case, and

[1] "Latent Gonorrhœa in the Female Sex, with Special Relation to the Puerperal State." By Dr. Angus Macdonald.—*Edinburgh Medical Journal*, June, 1873.

place by it for comparison one which came recently under my observation.

Case 13 (Dr. Angus Macdonald's Case 1).—"Mrs. S., aged 24, was delivered of a female child after an easy labor, on the 15th of April, 1869. Previous labors two, and had been quite normal. Both mother and child did well until about the fourth or fifth day, when the mother was seized with severe pain in the abdomen, accompanied with great tenderness on pressure, and a considerable amount of fever. This pain and tenderness, however, disappeared in about a week or ten days, under the influence of opiates internally, and the application of poultices externally. About the same time as the mother became ill, the baby's eyes were noticed to be affected with severe conjunctivitis of a suspiciously specific character. On inquiry, I ascertained that the husband of my patient had, during the time she was carrying this child, been affected with discharges of a gonorrhœal character, but that she herself had not suffered in consequence, except that she had some leucorrhœa before her confinement. She had had no pain on micturition, nor any swelling of the parts, as far as she could remember. The child's eyes were treated." . . . The mother made a slow recovery, but was able to be out of bed by the end of five weeks. "About this time, after being at church getting her child baptized, my patient was suddenly seized with excruciating pain in the left side of the pelvis, about the situation of the left ovary, accompanied with quick pulse and fever. This, on physical examination, gave all the usual signs of a perimetritis originating near the opening of the left Fallopian tube, and spreading forwards and towards the right, so as to involve the anterior half of the pelvis, and fix the uterus in position. For this attack she was treated by poultices and opiates, as well as, latterly, with the bromide and iodide of potassium, and other remedial agents. She made an exceedingly slow recovery, and was more than six months almost entirely confined to bed. . . . Since then I have ascertained from her that she suffers more or less severely at each menstruation from pain in the left groin, and that when she menstruates she is usually ill for nearly three weeks at a time, though not very much blood comes away at any one time. Since I attended her, in 1869, she has given birth to two healthy children. . . . She is now in tolerably good health."

Case 14.—B. J., æt. 24, married two years and a half. Had one child a year after marriage. She came under my care owing to a chronic ailment, which was ascertained to be perimetritis, with double laceration of the cervix uteri. The anamnesis supplied the following facts:—The patient was well until her confinement; she had copious leucorrhœa during her pregnancy, but no urinary trouble. Two weeks after her confinement some severe inflammatory illness, affecting the abdomen, came on, and she was in bed several weeks. She has suffered from pain in the left iliac and inguinal regions more or less ever since. The child suffered from an inflammation of the eyes, with discharge of matter, for which it was successfully treated by the doctor in attendance on the mother. There have been several relapses since the patient's recovery from the first acute illness, the last dating from a fortnight before she came under my observation. In an interview with the husband, I learned that he had a gleet for over a year before his marriage, but considered himself quite cured for two months at least before the marriage took place. He observed, however, for a long time, that after sexual intercourse there used to be a moistening and adhesion of the meatus. This patient is still under treatment, and other facts of the case may have to be referred to in illustration of points which would at present seem irrelevant.

There can be no doubt that the case is one of late gonorrhœal puerperal fever, and the course of the disease is that of a recurrent perimetritis. This is a fairly typical case, and the present purpose is served by placing it in juxtaposition to Dr. Angus Macdonald's typical case of early development of the inflammatory symptoms. But the relation of gonorrhœal infection to the puerperal diseases is too important to be treated only incidentally.

The late Dr. Thorburn, of Manchester, paid some attention to gonorrhœa in its relation to gynæcology, but soon concluded that it was unimportant. At the meeting of the British Medical Association held at Manchester in 1877, he read a paper on "Latent Gonorrhœa as an Impediment to Marriage," of which a too concise summary is given in the *British Medical Journal*, of August 25th, 1877. Dr. Thorburn denied the possibility of Noeggerath's conclusions being correct, and "appealed to the statistics of 81 private families, carefully

collected by him. He showed that there had been 33 per cent. of male gonorrhœic infections previous to marriage, 26 in all; and taking all the cases of abortion, sterility, uterine, and pelvic inflammations, and living births that had occurred in these eighty-one families, he showed conclusively that there had been the merest fractional difference in their proportion between the previously and not previously infected classes. As regards inflammatory pelvic affections, the balance was fractional in favor of the free gonorrhœic cases; in other respects equally fractional in favor of the non-gonorrhœic." The conclusion was that the latent gonorrhœa of Noeggerath is mythical; and is not, as it otherwise would be, an imperative barrier to marriage. It is not for me to go behind the statements here quoted and try to explain them away or minimise them. They do not seriously affect the question whether or not gonorrhœa may be an important factor in the causation of the diseases with which the gynæcologist has to deal. It must at once strike the reader, possessed of local knowledge, that Dr. Thorburn's statistics would be drawn from a class of people, exceptional to some extent in this respect that they would be specially careful and cleanly in their habits, and specially careful of their own health and that of their families, reducing to the minimum both the chances of contagion and the consequences of contagion, if perchance it did occur. However, I am concerned at present only in giving illustrations of the clinical work done under the influence of Noeggerath's "grand idea," and before the discovery of the gonococcus. We come now to the work of Neisser.

Neisser's Discovery and its Influence on Research and Observation.

So early as 1869, Hallier[1] had discovered and described the cocci which occur in gonorrhœal pus, but in the absence of sufficient means of magnifying, coloring, and illuminating the objects examined, his work attracted little attention.

In 1879, Dr. Albert Neisser,[2] at that time assistant in the

[1] *Zeitschrift für Parasitenkunde*, 1869. Bd. I., p. 179.

[2] "Ueber eine der Gonorrhoe eigentümliche Micrococcusform."—*Centralblatt für die medicinischen Wissenschaften*, 1879, No. 28.

University Clinic for Dermatology at Breslau, published an account of his observations. Whatever suggestions may have been thrown out by previous investigators, there can be no gainsaying the fact that it was Neisser's publication which gave the stimulus and guidance to workers in the same field, and has led to an ever-increasing and widening process of research and experiment, by both clinicians and biologists.

Neisser found that when he prepared the pus of gonorrhœa in a certain way, he could see, in and about the corpuscles, micrococci, which he concluded must be characteristic of the disease. He put the thinnest possible speck of pus upon the object glass, and allowed it to dry; he then stained the pus with a watery solution of methyl violet, and allowed it to dry once more. It was then ready for examination. In his investigations, Neisser used a Zeiss's microscope with Abbé's illuminating apparatus, $\frac{1}{12}$th oil immersion lens, with ocular No. 4 or 5. On bringing the object into focus, besides the nuclei of the pus cells, varying in form and deeply stained, while the protoplasm took on the dye but slightly, there could be seen more or less numerous groups of micrococci. Single individuals were seldom to be seen; almost always there were two micrococci so close to each other as to give to the observer the impression that they were one organism. He described each double individual as forming a figure-of-eight, or as a pair of dinner-rolls placed with the flattened surfaces close to each other. He believed that they developed by a process of division, each half of the double organism gradually dividing and forming a fresh double organism. This process is shown in diagrammatic form in the accompanying illustrations taken from Bumm's work (Fig. 2c). The micrococci for the most part formed colonies of 10, 20, or more individuals, and they were surrounded by a mucous envelope, which could be distinctly seen under a more subdued light. The micrococci were found chiefly on the surface of the pus corpuscles, rarely on the epithelial cells. In some pus corpuscles which were beset with micrococci, the nucleus was wanting or diminished in size.

Neisser, at the time of publishing his first essay, had found the micrococcus in 35 cases which he had examined. In every case examined this was the only sort of micro-organism found in the gonorrhœal pus, with the exception of a case which was suspected from the first of being complicated with soft chancre

of the urethra. On the other hand, this particular micro-organism was not present in the pus from every other form of venereal disease or complication. Nor could it be discovered in any one of thirteen cases of simple fluor vaginalis submitted to examination without selection.

Exactly the same typical micrococci of gonorrhœa in the male were found in nine cases of purulent urethritis in women. In the seven cases of purulent ophthalmia of the new-born, which had so far come under examination, the same characteristic micrococcus was found in great abundance. In all cases of simple conjunctivitis, which were examined for the sake of comparison, the micro-organism was looked for in vain. It was present in the only two cases of gonorrhœal ophthalmia in the adult which had come under observation.

The presence of the micrococcus consequently appeared to Neisser to be a constant mark of a gonorrhœal affection of the urethra, and of the eye; and even at the time of publishing his observations, he had repeatedly made use of this fact in order to diagnose the specific gonorrhœal character of pus.

The publication of this discovery in Germany, at a time when Koch's countrymen were full of confident expectation as to the future of the new bacteriology, attracted to it universal attention, and brought a host of workers into the field. It was not to be expected that the results of all observers would agree, and the history of seven years' industrious observation and experiment shows a good deal of difference of view on even essential features of the subject. Neisser himself has been constrained to modify his original opinions, but, upon the whole, his work has been only supplemented and established by subsequent observers. The reader to whom the subject is comparatively new, when endeavoring to get at that which is acquired and added knowledge, amid a good deal of conflict of evidence, even in matters of fact, should not be discouraged into relinquishing the quest. He should remember that while most of us look upon Jenner's discovery as one of the greatest boons ever conferred upon mankind by medical science, there are still not a few who denounce it as a curse; and among these there are to be found men who have had the opportunity which a medical education offers of acquiring scientific modes of thinking, and so subordinating their emotions to their intellect when discussing scientific questions. Similarly, it will be

possible, I think, to trace in the work of some contributors to the elucidation of the questions arising from Neisser's discovery, the influence of fixed and rooted opinions, and perhaps also of bias of even less creditable origin, in judging of new facts.

As Neisser's discovery emanated from a clinic for dermatology, the dermatologists and syphilologists were among the first to publish observations. The presence of the micro-organism in the opthalmia of the new-born interested the ophthalmologists and obstetricians, and other inquirers soon followed suit. It seems to be the custom for the specialists in Germany to publish their results, for the most part, in their special journals, and so the literature of a subject such as that under consideration, which claims the attention of several specialists, is almost inaccessible to the foreigner. Bumm, of Würzburg, whose work we must chiefly draw upon, mentions fifty-two contributions up to the beginning of 1886, and I find forty papers on ophthalmia neonatorum alone abstracted in the *Centralblatt für Gynäkologie,* in the six years 1881-86, some of them, like Credé's, being considerable treatises. It is only possible, therefore, in trying to get a clear view of the present state of opinion on all that relates to the gonococcus, to select merely the contributions which have added something to our knowledge and have stood the assay of criticism and later experience.

In 1880, A. Bokai[1] published the results of attempts to cultivate the micro-organism. He succeeded in obtaining pure cultivations, and in two cases he believed that he was successful in producing acute gonorrhœa in men by transferring a few drops of the fluid containing the crop of pure gonococci to the urethra. In the same year F. Weiss,[2] of Nancy, prepared a thesis, under the guidance of Prof. Spillmann, in which he described afresh the organisms observed in gonorrhœal pus, and alleged that it was constantly found in a large series of cases.

Haab,[3] who has published at least two important papers on

[1] "Ueber das Contagium der acuten Blennorrhoe."—*Allgemein. med. Central Zeitung*, 1880, No. 74.

[2] Weiss: Thèse: Nancy, 1880. Published in *Annales de Dermatologie*, 1881.

[3] Haab. *Korrespondenzblatt für schweizer Aerzte*, 1881, Nos. 3, 4; and same Journal, 1885, Nos. 1, 2.

the ophthalmological aspects of the subject, found the cocci of blennorrhœa neonatorum absolutely identical with those of gonorrhœa. He met with the figure-of-eight coccus constantly in the virulent inflammation of the conjunctiva, and as constantly failed to find it in the pus produced by simple catarrh. In the second paper, which is devoted to the "Etiology and Prophylaxis of the Ophthalmo-blennorrhœa of the New-born," he says that he recognizes the disease as of gonorrhœal origin only when he has made out by the microscope the presence of gonococci. Ordinary vaginal and lochial discharges do not produce blennorrhœa, but a simple purulent catarrh; without the microscope the differential diagnosis is impossible in the early stage.

After several of the ophthalmologists had published their observations, all of them adding to the proof of the justness of Neisser's original statements, Neisser[1] himself again came forward with the results of more mature investigation. He maintained that the gonococcus is a distinct organism, both functionally and morphologically. He again described its size and shape, and explained that its occurrence always in masses or colonies, never in chains, depends upon its mode of development, which is by a process of division at right angles to the long diameter of each element of the double individual. It is absolutely constant in every gonorrhœal inflammation of a mucous membrane, and it occurs in no other disease. He had succeeded in obtaining pure cultivations of the organism.

About the same time an important contribution to the subject was made by Leistikow,[2] assistant in the Clinic for Syphilis in the Berlin Charité Hospital. He failed to find any bacterium characteristic of hard or soft chancre, but he was able to demonstrate the occurrence of Neisser's gonococcus in the gonorrhœal inflammation of all the mucous membranes. He found that the gonococci were not on but inside the pus corpuscle, and that the development of a large number of them caused bursting of the cell-wall. His attempts at inoculating

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[1] "Die Micrococcen der Gonorrhoe."—*Deutsche med. Wochenschrift*, 1882, p. 279.

[2] "Ueber Bakterien bei den venerischen Krankheiten."—*Charite-Annalen*, VII., p. 750. Abstract in *Centralblatt für die med. Wissenschaften*, 1883, No. 22.

various animals with pure cultivations of the gonococci gave no result.

In the following year Bockhart,[1] of Würzburg, published a curious experiment, whose results introduce us for the first time to some acquaintance with the tissue changes produced by the development of the gonococcus. He obtained pure cultivations of the gonococcus, and he injected some of the fourth generation into the hitherto perfectly healthy urethra of a man in the last stage of dementia paralytica. Two days later the external orifice of the urethra was found to be slightly reddened, and a drop or two of a mucous secretion could be expressed. In the course of the two following days the scanty discharge had become purulent. On the fifth day a copious thin mattery discharge could be pressed out from the canal. From the third day onwards microscopic examination revealed the presence in the pus of innumerable gonococci. The patient died at the end of ten days, and thus Bockhart was enabled to make a microscopic examination of the diseased mucous membrane. He concluded that the gonococci are the pathogenic bacteria of the gonorrhœal diseases. When brought into contact with urethral mucous membrane they penetrate, probably between the epithelial cells, into the lymph spaces of the mucosa and submucosa of the fossa navicularis; here they multiply and give rise to active inflammation and migration of white blood corpuscles. They enter the white blood corpuscles, and penetrate with them into the blood vessels and push on in the connective tissue of the mucosa and pars cavernosa upwards towards the bladder. They destroy the white corpuscles into which they have migrated, and are themselves ultimately destroyed in the tissues or in the blood stream. Thus far, observers are unanimous in their agreement with Neisser, but now Sattler and Eklund, working at different subjects, announced their opinion that the micrococcus cannot be specific. The former concluded that he had obtained the characteristic, so-called specific gonococci, in the discharge from the eyes of a new-born child purposely inoculated with the vaginal secretion of an apparently healthy woman. The latter believed that he had found exactly similar

[1] "Beitrag zur Aetiologie und Pathologie des Harnröhrentrippers." —*Sitzungsbericht d. phys. med. Gesellschaft zu Würzburg*, 1883, Nos. 1 and 2. Abstract in *Centralblatt für Gynäkologie*, 1884, No. 36.

and apparently identical micro-organisms in other purulent discharges than those of gonorrhœa. Schirmer,[1] assistant in Sattler's clinic at Erlangen, has also mentioned one case in which typical blennorrhœa of both eyes came on in a new-born child from accidental contact of some vaginal discharge of the mother with one of its eyes. He says the mother was quite clean, but he does not refer to any microscopic examination of her discharges or to any attempt at cultivation of the organism in proof of the truth of his assertion. His evidence, therefore, becomes reduced to the "frivolous anecdote" rank, such as the reported cases in which men are alleged to have contracted specific urethritis from perfectly healthy women.

Of quite a different sort is the evidence of Zweifel,[2] then also of Erlangen, it may be noted. Lochial discharge, varying in time post partum from the 3rd to the 13th day, was taken from lying-in women who certainly had never suffered from gonorrhœa, and applied with certain precautions to the conjunctiva of healthy new-born children. The lochial secretion was first carefully examined microscopically for cocci, and a few cocci but no gonococci were discovered. The experiment was tried in six cases, and not only did no simple ophthalmia or specific blennorrhœa arise, but their eyes remained perfectly sound.

E. Arning,[3] working in Neisser's clinic, discovered the gonococcus in the discharge from the inflamed glands of Bartholini in eight cases of gonorrhœa. He colored the cocci with methyl blue and the cell protoplasm with eosin. He was of opinion that the gonococci were *in* the cells, but he dissented from Bockhart's statement that they penetrated the nuclei.

Amidst a series of papers emanating from various sources, but adding little or nothing to our knowledge, we come upon E. Bumm's[4] first contribution. His subject is gonorrhœa in women, and he announces the discovery, in the vaginal

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[1] "Die Augenentzündung der Neugeborenen."—*Centralblatt für Gynäkologie*, No. 14, 1882.

[2] "Zur Aetiologie der Ophthalmoblennorrhœa neonatorum."—*Archiv für Gynäkologie*, Bd. XXII., Heft 2.

[3] "Ueber das Vorkommen von Gonokokken bei Bartolinitis."—*Vierteljahrsschrift für Dermatologie und Syphilis*, X.

[4] "Beitrag zur Kenntniss der Gonorrhoe der weiblichen Genitalien."—*Archiv für Gynäkologie*, Bd. XXIII., Hft. 3.

secretions, of more than one diplococcus exactly similar in form to Neisser's gonococcus. The real pathogenic organism he could separate from the non-pathogenic only by means of pure cultivation. The substance of this paper is contained in the author's large work, which we have yet to examine, and we may therefore omit any further reference to this early production.

Kammerer[1] announces the discovery of the gonococcus in the fluid contained in the knee-joint in gonorrhœal rheumatism. But the evidence does not seem very conclusive. He mentions two cases, in both of which there was a history of injury to the joint, and the proof of the existence of either rheumatism or gonorrhœa is not satisfactory.

Kroner,[2] of Breslau, read a paper in the gynæcological section at the meeting of the German Natural Science and Medical Association at Magdeburg in 1884, in which he gave the results of observations on 92 cases of the ophthalmia of the new-born. He found gonococci in 63 cases, and in 29 cases he failed to find them, in spite of the most careful search. He therefore concluded that there are two forms of blennorrhœa of the new-born, but apart from the presence or absence of gonococci he cannot make out any clinical difference between the forms. Kroner leaves the theme of his observations without any very definite statement of opinion. The subject has yet to be worked out, and that can only be done where the material of a lying-in hospital and an eye hospital can be brought into comparison and carefully and patiently dealt with.

At the same meeting Sänger,[3] of Leipzig, brought forward the subject of "Gonorrhœal Disease of the Uterine Appendages and its Operative Treatment." He stated that the hope aroused by the discovery of Neisser, that in the gonococcus we should find a means of diagnosing chronic gonorrhœa, had proved to be vain. He held it as an established fact that gonorrhœa could exist without the demonstrable presence of gonococci. The absence of the gonococcus proved nothing against the gonorrhœal nature of the disease, whilst the

[1] "Ueber gonorrhoische Gelenkentzündung."—*Centralblatt für Chirurgie*, No. 4, 1884.

[2] "Zur Aetiologie der Ophthalmoblennorrhœa neonatorum."—*Archiv für Gynäkologie*, Bd. XXV.

[3] *Archiv für Gynäkologie*, XXV. 1.

presence of diplococci, in view of the occurrence of non-pathogenic forms, did not prove the gonorrhœal nature of the disease. If the cocci cannot be found, they may have been somewhere broken up, whilst a ferment produced by them may still be active; or they are absent from the secretion while present in the tissues; or there exists—and this would render the high degree of infectiousness of the comparatively trifling amount of secretion in latent gonorrhœa the most intelligible—a permanent form (Dauerform) of the gonococcus not yet discovered. He suggests, by way of analogy, Koch's discovery of the spores of the bacillus of splenic fever, unknown till then.

This contribution of Sänger's, to which, as well as to the more mature essay already quoted from, reference will have to be made again, seems to me a most important one. From my own experience, I should say that there can be little doubt as to the difficulty of finding the gonococcus in chronic gonorrhœa in women. In cases of only a few months' standing, most certainly gonorrhœal in their nature, which have been under treatment, it has been almost invariably impossible to discover the gonococcus, however numerous other bacterial forms might be. If this be established as a fact by general experience, the sooner it is recognized as a fact the better. Fuller knowledge of the life history of the organism must furnish the explanation, and may lead to notable practical conclusions. The absence of the gonococcus in old standing cases is in striking contrast to its uniform presence in acute or sub-acute cases in the invasion stage. But of this more has to be said in its proper place. It should be remembered, however, that Neisser[1] has found the gonococcus in a remarkably large proportion of old chronic cases in men, and further experience may produce similar results from the gonorrhœal catarrh of the cervix uteri. Westermark's discovery of gonococci in the exudation of salpingitis is not a case in point.

In 1885 we have, besides several papers of practical value, such as Oppenheimer's already referred to, a series of observations by E. Fränkel,[2] which as yet stand almost alone and

[1] "On the Contagiousness of Chronic Gonorrhœa."—*Transactions of the Congress of German Naturalists and Physicians at Strassburg*, 1885. Abstract in *Centralblatt für die med. Wissenschaften*, 1886, No. 32.

[2] "On the Results obtained from the Examination of the Secretion in Colpitis occurring endemically."—*Deutsche med. Wochenschrift*, 1885, No. 2.

unexplained. He found in the discharge from non-gonorrhœal colpitis in children, diplococci which were in every respect absolutely identical with the gonococcus. Fränkel's communication elicited a further contribution on this obscure subject from J. Cséri,[1] of Budapest, which, unfortunately, contains no results of the cultivation experiments referred to as having been instituted. The danger of infection from some cases of colpitis in children has been long well known to the staff of the Stephanie Children's Hospital, in Pesth. Since October, 1883, the discharges in 26 female children, varying in age from two to ten years, had undergone microscopic examination, and in every one a large diplococcus bearing a striking resemblance to Neisser's gonococcus had been found. Biologically both cocci appear to be identical. The contagiousness of the discharge is very great, and contact of it with the conjunctiva may lead to serious results. Cséri mentions the case of a short-sighted nurse, who, in syringing a child with colpitis, got her eye infected by accident, and lost it in consequence of conjunctival blennorrhœa.

Further observations on this subject were published by J. Widmark[2] in the same year. He merely states that he has found the gonococcus in eight cases examined, but he does not seem to have proved the identity of the micrococcus present with Neisser's gonococcus.

The most recent French literature on the subject of the gonococcus is summed up in Martineau's[3] work. The author has worked at the subject alone, and in company with Goguel, and is perfectly satisfied as to the existence and pathogenic nature of the gonococcus. He claims for Bouchard precedence of Neisser, by one year, in the discovery and description of the micro-organism. The observations and experiments made by the French physicians have been the same in kind, though not so extensive as those carried out in Germany, but no one is referred to as having failed to satisfy himself of the importance of Neisser's discovery.

This fact is in marked contrast to the import of the con-

[1] "On the Etiology of Infectious Vulvo-Vaginitis in Children."—*Weiner med. Wochenschrift*, 1885, Nos. 22 and 23.

[2] "Gonococci in eight cases of vulvo-vaginitis of children."—*Archiv für Kinderheilkunde*, VII.

[3] "Léçons cliniques sur la blennorrhagie chez la femme." Paris, 1885.

tributions from Italy. In that country several workers have submitted the results of their German contemporaries to a destructive criticism, and have sought to prove that the gonorrhœa diplococcus of Neisser, considered as the pathogenic element in blennorrhagia, does not exist.[1] The last of these, Giovannini, merely gives categorically a summary statement of conclusions derived from work in the Pathological Institute of Bologna. Until he has described the method by which his results have been obtained, we may suspend our judgment.

[1] De Amicis : *Revista clinica terapeutica*, March, 1884 ; and Giovannini : *Centralblatt für die med. Wissenschaften*, No. 28, Nov. 27, 1886.

CHAPTER III.

CONTEMPORARY PATHOLOGY AND THE "GONOCOCCUS-NEISSER."

We have now passed in review the history of Neisser's discovery, and the chief episodes in the course of the evolution of our knowledge of the subject which have modified the original conclusions with regard to the morphology and functions of the gonococcus. Setting aside in the meantime the objections which have been raised on the basis of more or less complete and mature investigations, and accepting provisionally the broad conclusion that the gonococcus is the active agent, the pathogenic element, in the production of the gonorrhœal diseases, whether they affect the sexual organs of the adult or the conjunctival mucous membrane of the new-born, we may now proceed to look at the organism more closely, and consider how we are to detect its presence and how we may bring our knowledge to bear upon the diagnosis and the treatment of disease. Some refinements with regard to morphologically similar micro-organisms, and the mode of differentiating them from the true pathogenic gonococcus, can be considered when we have become more familiar with the ordinary methods of looking for the bacterium.

In order to save frequent repetitions and references, I ought to state explicitly here that in writing this chapter I have constantly drawn upon the work of Dr. Ernest Bumm, of Würzburg, whose treatise[1] is by far the most important and original that has so far appeared upon the pathology of the gonorrhœal infections.

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[1] "Der Mikro-Organismus der Gonorrhoischen Schleimhaut-Erkrankungen 'Gonococcus-Neisser.'" 2d Edition, Wiesbaden: J. F. Bergmann, 1887.

Examination of a Suspected Secretion.

In a case of alleged simple urethritis in a man, of suspicious purulent discharge from the pudenda of a woman, or of conjunctival inflammation in a new-born child, how can the practitioner decide whether he has to deal with a simple catarrh or an inflammation of specific origin? He must look for diplococci in colonies or groups within the leucocytes or pus cells of which the discharge is composed. How is he to look? In order to be available as a practical clinical procedure, any method of investigation must be simple and rapid, like the process of testing urine for the presence of albumen or sugar. A difficulty in the way of popularising any process, is the cost of the apparatus, and the care required to keep it in good working order. A good microscope, with a $\frac{1}{12}$th homogeneous immersion lens, is an essential provision. My observations have been carried on or verified with a Zeiss's microscope, provided with Abbé's illuminating apparatus; the objective is a Powell and Lealand's $\frac{1}{12}$th oil immersion, and the eye-piece almost always Zeiss's No. 2 or No. 4. The ordinary apparatus and re-agents for microscopic work are supposed to be at hand in carrying out the following rapid clinical method of *looking for a diplococcus* in a suspected discharge.

A thin cover-glass, carefully cleaned, is held ready in a pair of suitable forceps, and a minute drop of the suspected pus is spread over a small area of its surface. This is quickly dried by holding it in the current of hot air high above the flame of a spirit lamp. Over the dry matter on the glass a drop of a concentrated alcoholic solution of methyl violet is let fall and allowed to spread. After a momentary pause, the superfluous solution is got rid of by turning the cover glass on edge and bringing it in contact with some clean blotting paper. The glass, now covered with a thin film of the dye-solution, is again raised for a few seconds above the spirit lamp, not long enough for it to dry. The dye is next washed away, as well as it can be, by bringing the cover-glass under a stream of distilled water from a wash-bottle. The cover-glass with the adherent stained film of discharge has now to be dried. The drop of water which adheres to it can be got rid of by bringing the object edgewise on to a piece of blotting paper as before, but still the glass remains wet, and even in the heat of the spirit-

lamp it will take perhaps a minute to dry. This time may be saved, without drawback to the preparation as far as rapid clinical inspection is concerned, by immersing the wet cover-glass momentarily in absolute alcohol, which should be kept in readiness in a suitable vessel, such as a small wide-mouthed stoppered bottle. When the water is replaced by the alcohol, the drying above the flame of the spirit-lamp takes only a few seconds. A small drop of Canada balsam, dissolved in benzol, is now let fall upon the centre of the cover-glass, which is at once applied to the slide, previously cleaned and warmed. The preparation is now complete and ready for examination. With a little experience of this method, and when the appliances are all held in readiness, the practitioner will find that this method of looking for diplococci takes little more time than the ordinary testing of urine. There are obvious objections to the process if it be looked upon as a method of scientific research, but that is not its object. A quantitative analysis of the sugar in urine by even the shortest process requires time, but a qualitative analysis can be, and has often to be, made in the course of a consultation. So it may be desirable to know, in the course of a consultation, whether a discharge contains diplococci, and if it does, the overwhelming probability will be that the case is gonorrhœal, the anamnesis and the clinical features being available to perfect the diagnosis. For the purpose in view the method of examination which I have described is sufficient.

Bumm, in the monograph already referred to, says that at the Würzburg Clinic for Obstetrics and Gynæcology, they take only two or three minutes to make the preparations. For staining a watery solution of magenta (fuchsin) is used: the secretion is spread *upon the slide* and prepared in nearly the same way as that just described. When it is finally dried, the examination is made without a covering glass direct in the oil for the immersion lens.

Neisser's original method of examination could not be finished in one day because of the slow process of drying and staining, and Eschbaum's rapid method takes twenty minutes or half-an-hour. No process requiring such a length of time for its completion is suitable for the consulting-room, however admirable results it may afford in the pathological laboratory.

If it be desired to retain specimens for repeated examination

and reference, all that is further required in the preparation of them is to employ a saturated solution in aniline water of the dye-material selected, and to take plenty of time in drying.

Now the next question is: What do we see in the examination of an object prepared as described? If there are gonococci in the field they will be distinctly seen. When absolute alcohol is used to promote rapid drying, the staining material may be found to have spread a little into the intercellular spaces, but not so as to interfere appreciably with the efficiency of the process. In Fig. 1 we have an attempt to represent the field of view, in a slide prepared from a real case, that of a young man who had been declared cured of a gonorrhœa a

Fig. 1.

month before he came under examination. He was exactly in the condition in which men used to receive, and perhaps do still receive, medical sanction to marry. In consequence of "taking a glass of beer," he had the slightest possible return of discharge, and a speck of sero-purulent fluid supplied the object which the figure is intended to represent. It will be seen that the leucocytes are for the most part merely stained, and free from diplococci, the nuclei taking on a deeper coloration than the protoplasm. One epithelial cell occurs in the field. The diplococci appear only as black dots, for the most part double, but not uniformly so. Some observers see a good deal more of detail in the individual organisms, but no refine-

ments are to be expected from the rapid mode of preparation of the object. The appearance is, however, characteristic and unmistakable. In addition to the groups in or about the cells, it will be seen that two larger diplococci are visible with the epithelial cell as a background. These have probably fallen away from some disintegrating group; but, whatever be their origin, they are a common enough feature in the field of view in the ordinary course of searching a preparation for the gonococcus.

The illustrations in Fig. 2 are intended to show the relation

Fig. 2.—*a*—This group contains: 1, a normal pus corpuscle; 2, a pus corpuscle partly surrounded with cocci; 3, a pus corpuscle with cocci in the protoplasm; 4, a pus corpuscle completely filled with cocci, and 5, a free colony or group of cocci. *b*—Gonococci from a pure cultivation. *c*—A diagrammatic representation of the development of gonococci. *d*—Section from the conjunctiva, showing the presence of gonococci in the discharge before penetrating the epithelial covering.

of the micro-organisms to the other elements that come into view in the field during examination, and also to show some of the details which should be made out by the observer after employing more careful modes of preparation than that just described. They are taken from Bumm's work, and are, as he explains, mostly diagrammatic. The explanatory notes sufficiently indicate the various relations of the micro-organism to the tissue elements, which may be seen in preparations of gonorrhœal pus.

It may now be asked: If in examining a discharge by the method described, the observer finds diplococci in groups or

colonies, such as those figured above, is he justified in giving a decided diagnosis of gonorrhœa? Unfortunately the subject is not so simple as this, and a definite unassailable conclusion is not to be reached by such a summary process. In a suspected case, the discovery of diplococci arranged in the manner which has been described, makes it almost, but not altogether, certain that the disease is gonorrhœal. How then can we be certain? This brings us to the consideration of the diagnostic value of the presence of the gonococcus, and of a method by which it can be infallibly differentiated from any other micro-organism.

There can be no doubt that Bumm has proved the existence of micro-organisms which cannot be distinguished by the individual form alone from Neisser's gonococcus. He describes five different varieties of diplococci obtained by pure cultivation, only one of which, producing a yellowish-white film in the cultivation medium, is pathogenic. It is obvious that cultivation experiments cannot become a clinical method of differentiating micro-organisms which are identical or very similar in form, and we must therefore look for some more practical method. Such a method appears to have been discovered by Dr. Gabriel Roux,[1] of Paris. It depends upon the effect of Gram's staining fluid upon micro-organisms in general, including the diplococci resembling the gonococcus, as compared with its effect upon the gonococcus itself. Roux's application of Gram's method of staining consists in first coloring the dried film of secretion which is to undergo examination with methyl-blue or gentian violet, fixing the color, if it is fixable, with Gram's iodo-iodide solution, and then washing with absolute alcohol, so as to decolorise the pus or leucocytes in the secretion. Gram's liquid fixes the color in all micro-organisms, as far as is known at present, excepting the gonococcus. Hence it follows that if the cocci, which have been observed in a specimen of discharge prepared in the ordinary way, completely disappear after the application of Gram's solution and washing with alcohol, they are Neisser's gonococcus. If on undergoing the same treatment they remain visible, that is, retain their color, then they are some other form of diplococcus; and the case from which they are derived cannot be pronounced gonorrhœal on the strength of the microscopic examination alone.

[1] *Le Concours Médical*, Nov. 13, 1886.

Roux's method has been submitted to a severe trial by Dr. Charles W. Allen[1] and Dr. Edmund C. Wendt,[2] of New York, and they both express confidence in it as an exact test. These observers have worked together, and though writing in different journals they practically give identical reports. Dr. Allen says: "We have examined pus containing a great variety of forms of bacteria, and find that, while the double coloration method brings out all other micro-organisms more beautifully than any other process we have employed, decolorisation removes the staining from the gonococci and causes them to disappear, while other micro-organisms are not decolorised. Here, then, we have a method which, when carefully carried out, appears never to fail, and has the great advantage of simplicity." The process of examination, as practised by himself and Dr. Wendt, is thus described: "A drop of pus is spread into a thin layer by pressing between two glass slides and allowed to dry in the air. A drop of a solution of methyl-blue in aniline water is now placed upon it for a moment, and washed off with a stream from a wash-bottle; a few drops of Gram's iodo-iodide liquid is then poured on, and allowed to remain for several minutes. This fixes the color on micro-organisms in general. Gram's liquid is now washed off, and while the specimen is still wet, a cover glass is placed upon it, and it is examined with an oil immersion lens. If micro-organisms resembling the gonococcus are found, we proceed to test them by decolorisation. The cover-glass is removed, and the specimen treated with absolute alcohol, until the color is as completely removed as possible. The cover-glass is replaced, and the specimen again examined, when all gonococci will have been found to have disappeared. All other organisms, however, which may have been present will be distinctly visible. If desirable, the pus cells may be brought out again by applying a solution of eosin. By this method we have been able to exclude all cases which would have been of necessity left doubtful, without some confirming test."

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[1] "Practical Observations on the Gonococcus, and Roux's Method of Confirming its Identity."—*Journal of Cutaneous and Genito-Urinary Diseases*, March, 1887.

[2] "A New Color Test (Roux's) for the detection of the Gonococcus."—*Medical News*, April 23, 1887.

It has yet to be seen whether the experience of other observers will confirm Drs. Allen and Wendt in their confidence in Roux's test. Bumm is satisfied, from his experience of the behavior of the various organisms under staining processes, that the pathogenic diplococcus which he found in puerperal cystitis and in mammary abscess has its color fixed by Gram's staining fluid, while the gonococcus has not. But if Bumm's contention is well founded, there is still room for further evidence with regard to the behavior of the four other non-pathogenic varieties of diplococcus. Practically, in dealing with the discharges from the female genitals every source of error in identifying the gonococcus may be considered eliminated. If in a suspected case the particle of matter to be examined be carelessly taken from the lower portion of the vagina, there is a whole "fauna" of that region usually brought into the field of the microscope. But in every actual case for investigation, during the most characteristic and prolonged stages, the discharge for examination may be best taken direct from the orifice of the urethra or from the os uteri, and the fluid taken from either site is comparatively free from bacteria other than the gonòcoccus. I have constantly applied Roux's test for the last few months, and though as a test it seems satisfactory, I doubt whether, clinically, its application is not a mere counsel of perfection, only valuable in hushing quibbling and pedantic objections to the sufficiency of the clinical and ordinary microscopic methods of differentiation. Instead of examining the same film of mucus or pus first with the ordinary stain and again after the application of Gram's fluid, I have usually made six complete and permanent preparations from each specimen of discharge to be examined, and have labelled them so that they could be repeatedly compared, if necessary. Three of these preparations are made with the ordinary stain, one rapidly done, the other two more carefully; two others are prepared with Gram's fluid, washing in absolute alcohol, and mounting in Canada balsam as described; and the sixth is re-stained with eosin in order to make the pus and other cells again visible, as recommended by Roux. Without exception, in the cases ascertained to be gonorrhœal by independent evidence, when diplococci have been seen at all, they have disappeared under Roux's process, and this has been so whether the pus has been taken from the cervix uteri and been free from other bacteria, or from the

vagina when the diplococci were associated with myriads of other bacilli and cocci which persisted in the preparation after the washing with absolute alcohol.

In old standing cases of gonorrhœal origin, and in doubtful cases, diplococci have hardly ever been seen in the uterine discharge, and when they have occurred in non-gonorrhœal cases they could never be mistaken for the gonococcus, if the grouping of the gonococcus be characteristic.

With regard to the identification of the gonococcus in the actual clinical work of gynæcology, we are now in a position to collect the points of the complete process. They are:—

(1) The presence of some clinical sign or symptom to suggest the existence of comparatively recent infection.

(2) The collection of the secretion to be examined from the cervix uteri, from the orifice of the urethra, or exceptionally from the orifices of Bartholini's glands. As there is, strictly speaking, no vaginal blennorrhagia, the collection of the discharge from the vagina is merely inviting the risk of error.

(3) The presence of a diplococcus *in* the protoplasm of the pus corpuscles, or other elements of the fluid, and its arrangement in the groups or colonies which have been proved to be characteristic. A single group in the field of the microscope is sufficient to settle the question. In the absence of such a group, however numerous separate diplococci or groups of diplococci apart from the cells may be, we cannot pronounce the case to be gonorrhœal, even though we know that separate individuals and groups are very numerous in the acuter stages.

(4) Roux's test may be applied to complete the proof: (*a*) When all the other conditions of the proof are already fulfilled, in order to observe the disappearance of the gonococci, and (*b*) when some diplococci are present, but not in the characteristic groups, in order to see whether the persistence of the micro-organisms will prove the negative.

Presence of the Gonococcus—Its Clinical Significance.

The whole subject is in too inchoate a state to make it safe to allege that these conditions are sufficient to satisfy the requirements of medico-legal investigation. Clinically, so far as my experience goes, the fulfillment of the first three condi-

tions has justified me in stating that a disease was gonorrhœal when such a possibility was denied by the patient or by one of the parties to its production, and, *without exception*, the confident statement of the opinion has elicited information that was previously withheld. But this is anticipating what we have next to consider, viz., the diagnostic value of the presence of the gonococcus in a discharge. All experience goes to show that the presence of the gonococcus settles the question; it is the pathognomonic sign of the disease. Even the apparent exceptions support this conclusion. *If gonococci are present in the discharge from an inflamed mucous membrane, the discharge is of gonorrhœal origin.* Apparent exceptions to this rule have already been referred to. On the one hand, there are the reported cases of vulvo-vaginitis of young children, in which diplococci were observed, which could not by any means be differentiated from the true gonococcus. The later observations of Cséri, during an epidemic in Budapest, point, however, strongly to the conclusion that the virus of that disease and of the gonorrhœa of adults is identical. On the other hand, we have Kroner's observations on cases of ophthalmia neonatorum, in which the gonococcus could not be found in the discharge. Bumm's experiments, however, prove that the discharge from such cases is not infectious, and the inflammatory process is not followed by the same results as are seen in the genuine infectious ophthalmia of the new-born. Further inoculation experiments by Bumm with the discharge from the cervix uteri left as an effect of a former gonorrhœa, and with other discharges of gonorrhœal origin, but free from gonococci, the experiments of Zweifel with the vaginal discharges of puerperal women upon the eyes of the new-born, and a host of other experiments with every variety of discharge, lead us inevitably to the further conclusion that *a secretion containing gonococci, when brought into contact with a mucous membrane capable of infection, gives rise with certainty to a gonorrhœal inflammation;* and conversely, *a secretion, whatever its origin may be, which does not contain gonococci, is incapable of giving rise to a gonorrhœal inflammation.* The portion of the proof of these propositions, which consists of inoculation experiments with gonococci, derived from pure cultivations, is worthy of more detailed statement. The successful inoculations on the human

subject have been, from the nature of the case, very few; attempts to inoculate the lower animals have been uniformly unsuccessful. Gonorrhœa seems to be a purely human development. We have seen under what circumstances Bockhart's inoculation experiment was carried out; let us examine one of Bumm's more satisfactory experiments.

The original virus was obtained from a case of blennorrhœa neonatorum, and the inoculation was effected with gonococci of the second generation of pure cultivation in blood-serum. A speck from the cultivation area, along with a little clot of the serum, was conveyed by means of the platinum wire into the urethra of a woman, measures having been taken to prevent the spread of the disease, should it arise, to the internal sexual organs. The greatest care had been taken to ascertain that the genitals of the subject were entirely free from gonococci. Two days passed after the inoculation without any symptoms. On the third day the patient complained of a burning pain in micturition, and a small amount of yellowish watery secretion could be pressed from the urethra. This discharge contained separate gonococci as well as groups upon the epithelium. The other numerous pus corpuscles present were quite free from cocci. Next day the urethral mucous membrane, which had become red and swollen, bulged out from the orifice. The secretion was now thin, purulent, and small in quantity, and it contained numerous free cocci, epithelium cells beset with cocci, and also some pus cells filled with them. The further course of the disease was that of a rather severe attack of urethral gonorrhœa. The acute stage lasted three weeks, and the discharge required other three weeks of treatment to bring it to a complete cessation. No complications occurred. The discharge was regularly examined during the whole course of the attack, and the presence of the gonococcus in the characteristic manner was as regularly demonstrated. An almost exactly similar experiment was made with the twentieth generation of a pure cultivation of the gonococcus with a similar result.

These inoculation experiments of Bumm's fulfill all the requirements of a complete proof that the micro-organism is the cause of the disease. We have in them (1) a distinct type of disease in gonorrhœa; (2) the isolation of the organism developed in that disease, and its cultivation in artificial

media apart from the tissues in which it originally developed; (3) the inoculation of the organism into tissues capable of taking on the diseased action, and the production thereby of a disease characterised by all the phenomena of the original disease; and (4) the identification of the micro-organism in its characteristic relation to the tissues undergoing the diseased process set up as the result of inoculation.

If the proof, as stated so far, has done justice to the available material for proof which exists, we should now be in a position to accept the dictum—*without the gonococcus there is no gonorrhœa;* and, conversely—*without gonorrhœa there is no gonococcus.* The truth of these propositions is far-reaching in its influence. Gonorrhœa is the only disease which produces an infectious catarrh of the female genitals. All the various other diseased conditions and irritations producing catarrh of the genital tract in the female, which have been alleged to give rise to urethritis in the male, must be admitted to be innocent; they cannot produce a specific blennorrhœa. What then, it will be asked, becomes of the cases with which we are all familiar? We have all seen men who have had the alleged misfortune to contract a urethral inflammation from their wives; they have indulged too imprudently in sexual intercourse; the wife has a chronic discharge from general bad health, or from the mechanical irritation of a pessary; she had not quite ceased menstruating, and so forth. It is an ancient and convenient superstition, which has been almost universally accepted as fact. For such facts so much the worse if they do not square with the well-established modern doctrine. That a simple urethritis, *simulating gonorrhœa,* is not possible, it would be illogical and absurd to allege; but that few of us ever see such a urethritis, whose origin is above suspicion, the universal experience must admit to be the fact. When we consider, on the one hand, how rare alleged simple urethritis is, and how common the specific form; and, on the other hand, how frequently, one might almost say universally, some amount of uterine or vaginal catarrh is found among parous woman, who have never run the risk of specific catarrh, we must admit that there exists a discrepancy which is inexplicable on any hitherto accepted theory. If simple urethritis in the male could be produced by any form of non-specific catarrh in the female, then urethritis would be one of the

commonest of ailments among continent married men, just the class among whom it is seldom or never seen. No case of alleged simple urethritis need, however, cause more than a momentary difficulty. Such cases are always seen in the acute stage; if the discharge contains gonococci, it is specific; if it is free from gonococci, the inflammation is not gonorrhœal. This facility for learning the truth may be sometimes embarrassing to some patients, and occasionally to the practitioner; but the existence of an exact criterion in the early stage cannot fail, in the long run, to conduce to the morality and to the physical well-being of the community.

A case which well illustrates these points has recently been under my care. It was that of a lad of sixteen, a member of a highly-respectable family, who was brought to me by his mother. He had recently come home from school, and he had not been able to conceal the fact that he was suffering from a discharge from the penis. On examination I found that he was the subject of marked phimosis, and the orifice of the urethra could not be brought into view. The purulent discharge from the opening of the prepuce was copious enough. Not so long ago I might have been satisfied and silenced by the explanation which was given me as to the cause of the disorder. But I made a microscopic examination of the pus, and found typical gonococci. The possibility of my view, as stated to the patient alone, being correct was at first strenuously denied, but while he was under treatment I ascertained the origin of the malady. There was nothing unusual about it.

The occurrence of ophthalmia in a new-born child should also lead to an examination of the discharge. If the matter contains gonococci, the disease is gonorrhœal, and in the absence of proof of post-partum infection, it is to be presumed to have originated in gonorrhœal infection of the mother. This is now a universally accepted opinion, and the facts calls for no further notice.

Development of the Gonococcus in the Tissues—Its Effects.

The immediate dependence of the phenomena of the gonorrhœal inflammation upon the presence of the gonococcus

brings us to this conclusion, that the pathology and pathological anatomy of this disease are described in any satisfactory account of the life-history of the gonococcus and the changes which its development produces in the tissues which harbor it. We have seen incidentally the result of Bockhart's experiment on the urethra of a dying paralytic, and the pathological investigation of the condition of the mucous membrane. Bockhart's conclusions have been warmly contested, especially with regard to the extraordinary penetrative power of the gonococcus, and its capacity for migration. But from the nature of the case there are few in a position to speak with confidence on the subject. Very few opportunities occur of submitting to sufficiently searching examination the urethral mucous membrane when it is in the condition to throw light on the pathology of gonorrhœa, and no opportunity at all of observing the progress of the disease in the urethra from day to day. The principal work of pathological investigation has been carried out upon the conjunctiva of the new-born; and here Bumm's[1] contribution stands out pre-eminent. Bumm had the opportunity of snipping out a small portion of the conjunctiva in a large number of cases of ophthalmia neonatorum at different stages of the disease. These portions of tissue were prepared and submitted to careful microscopic examination; and the observations thus made cannot fail to throw much light upon the minute anatomy of the disease-process in the genital tract. His observations extend from the first to the thirty-second day of the disease, when the gonococci could no longer be found either in epithelium or in connective tissue. The knowledge derived from a short summary of Bumm's conclusions may be advantageously applied analogically to the phenomena of the disease as observed in the female sexual organs. It will be found to explain some clinical features otherwise obscure or inexplicable, and to suggest a reasonable explanation of some symptoms of whose causation we have at present no direct knowledge.

Along with the infecting secretion at the outset of the purulent ophthalmia infection, there comes in contact with the conjunctival sac a small number of the micro-organisms. These find in the superficial moist layer of the conjunctiva an excellent soil, and proceed at once to proliferate, so that in

[1] *Loc. cit.*

twenty-four hours from the first contact they may be found in great abundance. While other micro-organisms which may have been brought incidentally into the conjunctival sac, amidst the infecting secretion, are rapidly eliminated by the movements of the eyelids and the flow of tears, the gonococcus holds its ground. "Endowed with an eminent invasive force," it penetrates between the superficial epithelial cells, and also into the soft protoplasmic substance of the same elements, continues to proliferate between the layers of the epithelium, and ultimately reaches the papillary layer of the mucous membrane. There is no evidence that the micro-organisms possess any power of locomotion to carry them against the outward stream of fluid. They develop superficially and inwards, probably owing to something in the nature of the soil. The time taken by the process varies to some extent, but usually in two days the micro-organism has penetrated and taken complete possession of the whole epithelial sheath. The way in which it marches forwards is always the same—by breaking down the cementing substance between the epithelium elements. Sometimes the gonococci are seen pressing forward in thin streaks, sometimes spreading out into rounded colonies or thinly scattered groups of fungi, according to the resistance of the tissues to be penetrated. In every case the reaction on the part of the tissues is at this time very energetic and complete. Great swarms of white blood-corpuscles migrate from the capillary network which comes close down to the epithelial sheath, penetrate into the superficial layers of the connective tissue, and thence find their way through the epithelial layers to the surface. Owing to the disintegration of the strata of epithelium by the development of the fungi, it gets carried away in the stream of fluid and of cellular elements, either as individual epithelium cells or in flakes, a breaking up to which capillary hæmorrhages between epithelium and connective tissue and the movements of the eyelids contribute.

At the verge of the transition-epithelium of the limbus corneæ and of the edges of the eyelids, the invasion by the fungi breaks off suddenly. This epithelium, as well as the pavement epithelium of the cornea, retains its regular stratification and normal appearance. It resists the invasive force of the gonococcus.

When the epithelial sheath is broken through, the papillary portion of the mucous membrane lies exposed to the ravages of the micro-organisms. But their invasive force appears to be broken; they penetrate only the most superficial sheath of the sub-epithelial connective tissue. Usually the gonococci lie in small groups in the interspaces between the strains of fibres which run parallel to the surface. More rarely they may be seen in streaks penetrating perpendicularly, and these possibly reach the capillary lymph-spaces.

While the micro-organisms are thus invading the superficial layers of the conjunctival connective tissue, the inflammatory process appears to have increased in intensity; the infiltration of round cells reaches finally as much as 2 mm. under the free surface of the mucous membrane, and the individual cells are crowded upon one another. This process gives direct origin to the purulent stage of the blennorrhœa.

The process of repair begins usually within four days, but it varies according to the severity of the attack. It starts from the remnants of the original epithelial covering, proceeds rapidly, and soon brings to an end the further development of the cocci in the tissues. The new epithelial sheath consists of a layer of cubical or slightly elongated elements, which becomes rapidly covered with two or three layers of flatter cells. The most superficial of these layers becomes further modified, and the whole sheath forms an impenetrable protection to the underlying tissues against the micro-organism. By the time the process of repair is well advanced, viz., the tenth or twelfth day, the gonococci are no longer present in the connective tissue, only in the superficial portion of the epithelial sheath, where whole ranks and groups of the micro-organisms still hold their ground. Occasionally there is a re-invasion of the deeper strata, when the new protective layers are broken through at points by the outward stream of *débris* from the surface of the connective tissue, and then there is a fresh invasion by the cocci, a repetition of the process, and, to some extent, of the appearances resulting therefrom. Such relapses hinder the process of repair, but do not prevent the complete development of the new kind of epithelium. The process of epithelium formation is usually complete in the third week of an attack of ophthalmia of the new-born, and the epithelial sheath remains intact during the subsidence of swelling and proliferation of elements in the papillary layer behind it.

The force of the invasion by the fungi and the duration of its different phases vary greatly in different cases. When the processes in the ophthalmia of the new-born were compared with the stages of the gonorrhœal ophthalmia in the adult, it was found that the process of repair was longer in beginning in the latter, and the invasion of the connective tissue of the mucous membrane was deeper, more extensive, and of longer duration. As late as the fourteenth day of the disease in an adult no trace of an epithelial sheath could be seen; the papillary portion lay completely exposed, and contained, to a considerable amount, colonies of gonococci, partly free and partly in the cell protoplasm of the pus corpuscles.

When we see the invasion by gonococci giving rise to such different phenomena according to the age of the individual attacked, we cannot reject, without further consideration, the view that when implanted upon such a suitable soil as the urethral mucous membrane of the adult, the gonococcus may develop more vigorously and penetrate more deeply than it has been shown to do in the conjunctiva of the new-born. It is not improbable, though there exists no direct proof except in the single case of Bockhart, that the invasion may extend to the lymph-vessels and even into the capillary blood-vessels, but such an occurrence must be the exception, not the rule. Bumm maintains that he has proved that the gonococcus can only invade and destroy cylindrical epithelium, it cannot enter the pavement epithelium, and it can penetrate only the most superficial layers of the connective tissue of a mucous membrane. Whether there is any essential difference in the mode and extent of invasion when the gonococcus develops in the mucous membrane of the urethra, of the cervix uteri, or of the Fallopian tube, remains to be proved by direct observation. As far as our knowledge of the process in the conjunctiva is concerned, we see that the reaction of the tissues in the acute stage corresponds exactly to the violence of the onset and the rapidity with which the micro-organism is developed; and in the later stages, when the tissues have become protected by the development of epithelium due to the reaction of the tissues, and the gonococcus disappears, the remaining phenomena of the disease are just those which may be produced by any chronic irritation. The final process of healing depends not so much upon the elimination of the micro-organisms, as

upon the closing of the tissues against their further invasion, by the development of thick layers of pavement epithelium.

The application of these conclusions to the phenomena of the gonorrhœal process in the genital tract is so obvious that any attempt at an explicit statement would be superfluous. The reaction of the tissues leading to the development of a special modification of epithelium, which will ultimately become in some sense cicatricial, explains at once the modified symptoms of second and subsequent attacks of gonorrhœa; and there are other equally striking points in the fitness of the results of Bumm's observations to explain clinical features of the disease, as we must trace them in the sexual organs.

Theory of "Mixed Infection."

No account of the pathology of gonorrhœal infection would be complete up to the present time without mentioning in some detail Bumm's theory of mixed infection, which has been already hinted at. His most recent contribution is a paper[1] published in December last, which, we may take for granted, contains the most mature experience on the subject.

Mixed infection is defined as the invasion of the organism by two or more kinds of bacteria. When these mixed infections are accidental they deserve no further notice. But that kind of mixed infection in which there exists a causal connection between the invasion of the two germs is most important. In such a case the bacterium possessing the greater power of invasion precedes and, as it were, prepares the soil for the second germ. These forms of mixed infection are distinguished by a certain constancy of occurrence, and the possibility, and even probability, exists that if one germ has settled another will follow. Ordinary croupous pneumonia with its after diseases is a typical example. The bacteria of pneumonia deprive the alveoli of the lungs of their epithelium, and fill them with an exudation, which is a soil in which secondarily tubercle bacilli or pyogenous germs settle, and which may lead to the termination of the illness in phthisis or formation of abscesses. The gonococcus, too, by its growth on the mucous membrane of the female genital tract, is capable of so altering its substratum that other fungi which are usually present there

[1] "Ueber gonorrhoische Mischinfectionen beim Weibe."—*Deutsche medicinische Wochenschrift*, No. 49, 1887.

without doing harm, or which, favored by suppuration, find their way from the air, obtain an entrance into the tissues, and then on their own behalf exert their specific effects, which are totally different from those of the gonococcus.

This fact is well illustrated in the gonorrhœal infection of the vulvo-vaginal glands. These and their ducts are tolerably frequently the seat of gonorrhœa in women. The ordinary course is this: an acute purulent stage is followed by a chronic mucous discharge, which may continue for months. The secretion gradually ceases, part of the gland becomes destroyed, and finally cure supervenes. The course, however, is totally different if, during the course of the acute blennorhœa, pyogenous micro-organisms find their way into the inside of the gland. The previously only tolerably tender gland becomes painful and swells, the skin covering it becomes red, and soon the appearance of purulent Bartholinitis is produced.

Such a gland, excised and examined, shows no traces of gonococci. The pus inside the gland only contains pyogenous staphylococci; these have overpowered the gonorrhœa microbes, have penetrated into the gland-sac, and from there into the periadenitic connective tissue. This is covered thickly with heaps of cocci, and shows the first commencements of purulent liquefaction.

The great majority of all abscesses of the vulvo-vaginal glands are due to this kind of gonorrhœic mixed infection. Other fungi possessing no pyogenous properties may invade the gland without giving rise to any characteristic tissue reaction. Similar processes occur in the mucous follicles of the female urethra.

Catarrh of the bladder is another form of gonorrhœic mixed infection. Gonorrhœic cystitis does not exist in the sense that the specific cocci of gonorrhœa attack the epithelium of the bladder, as they do that of the urethra, and then cause it to suppurate. Bumm has isolated the active agent in cystitis—a special kind of coccus which is very similar to the ordinary gonococcus.

Returning to the genital tract, the inflammatory processes which, after cervical and uterine gonorrhœa, usually develop in the pelvic connective tissue and pelvic peritoneum are extremely frequent. Bumm says: "It is astonishing with

what frequency here (Würzburg), in gonorrhœa patients, in whom indeed excesses of all kinds, continuous mechanical insults, &c., but often also a too heroic (eingreifende) treatment tend to help, para and perimetritic processes are found." The microbes of gonorrhœa do not directly invade the lymph tracts and the connective tissue about the uterus, and cause inflammation and exudation. The territory of the gonococcus is fortunately limited to the superficial layers of the mucous membrane. Gonorrhœic para and perimetritis cannot be explained by the action of gonococci; there must therefore be another agent, which, under the influence of the infection of the mucous membrane, passes into the parametric tissues and there causes disturbance. It is not very common for that exudation to break down into pus; if it does so, the occurrence is due to mixed infection. Bumm has had two such cases: in one he demonstrated the staphylococcus pyogenes aureus; in the other, the noxious agent was a chain micrococcus. In both cases the formation of pus was doubtlessly due to the pyogenous micro-organisms, which found admission through the infected and eroded cervical mucous membrane, and settled and multiplied in the lymph spaces of the broad ligaments till they were eliminated by the purulent inflammation. Bumm thinks himself, therefore, justified in saying, "Purulent parametritis with gonorrhœa of the cervix is due to a mixed infection with pyogenous bacteria; it is the analogue of the acute gonorrhœic bubo in the male, which likewise owes its origin to pyogenous germs."

The further the gonorrhœal infection advances upwards from the cervix, the fewer admixtures occur in the gonorrhœic pus. In gonorrhœic uterine secretion, besides the gonococcus, but very few other bacteria are found, and they are scarcely ever found in the Fallopian tube. The gonococci advancing along the mucous membrane ultimately reach the tube, while other germs remain behind.

The proper character and the results of the pathogenous activity of the gonorrhœic microbes is therefore seen—pure and unadulterated—in the tube. They cause purulent inflammation of the mucous membrane, but the surrounding connective tissue remains free from them. The gonorrhœic tubal pus is evacuated into the peritoneum, and whereas in other conditions the bursting of an abscess into the abdominal cavity

is followed by the gravest consequences, in this case the whole process terminates with a circumscribed inflammation, encapsuling the exuded pus. The cause of this difference is the varying pathogenic value of the organisms which are contained in the pus. A puerperal pelvic cellulitic abscess bursting into the peritoneum causes general peritonitis, because it contains pyogenous streptococci, which rapidly multiply in serous cavities, and are capable of exerting the most deleterious effects. Gonorrhœal tubal pus cannot do this: its microbes do not find in the peritoneum conditions for their increase: the pus, therefore, acts as an aseptic body, becomes encapsuled, and is finally absorbed.

It may, under special circumstances, be possible for pyogenous cocci to get mixed with gonorrhœal pus, the result being a dangerous peritonitis. But such cases are as yet unknown or unreported.

Bumm then mentions another form of gonorrhœal mixed infection, viz., that with tubercle bacilli. Statistics, which are however few, and therefore not to be quite relied upon, seem to show that in the etiology of localised genital tuberculosis, gonorrhœic processes, especially epididymitis, play a *rôle*. The question arises whether the cases of isolated tubal tuberculosis are not due to an old tubal gonorrhœa. The thickened tubal pus, in which the gonococci gradually become disintegrated, might be a good soil for the tubercle bacilli, and so, by means of mixed infection, a tubal gonorrhœa might be changed into a tubal tuberculosis. He mentions the facts of a case which seem to support this opinion.

In the paper of which the above is a summary, Bumm frequently refers to parametritis as a result of gonorrhœal infection. It may be as well to take this opportunity of stating that hitherto my experience has not brought me a single case of parametritis in which there was the slightest evidence that gonorrhœal infection, pure or mixed, had anything to do with its production. While perimetritis is one of the commonest of complications, if indeed it is not part of the normal course of the disorder, parametritis must be among the rarest.

CHAPTER IV.

CLINICAL PHENOMENA OF GONORRHŒAL INFECTION IN WOMEN.

Coming now to the clinical phenomena of the disease, we shall see how far our modern doctrine of the pathology furnishes a feasible and sufficient explanation of the clinical signs and symptoms, and also to what extent our knowledge requires to be supplemented. It is not intended to reproduce here a description of an attack of gonorrhœa in the female such as might be suitable for a systematic treatise on the subject, but rather to describe and call attention to some features which are of value in relation to the diagnosis and treatment of the disease, but which, as a rule, do not attract sufficient attention. At this stage the description of subjective symptoms is purposely omitted to prevent repetition when we reach the illustrative cases which will be introduced.

There are two distinct types of the gonorrhœal disease in women: (1) the acute, and (2) the chronic or "creeping."

In the Acute Form.

The acute form, as affecting the urethra, does not differ materially from the gonorrhœal urethritis of the male. There is the same reddening, swelling of the mucous membrane, itching and burning, and finally the same discharge and scalding in micturition. The troubles in the female are less, as a rule, than in the male, and the complications of the urethral form less serious. Hence the comparatively little notice the disease received while the urethral affection was believed to be the most important part of the series of phenomena which ordinarily result from infection. In most of the cases to which I shall have to draw attention, the urethral troubles passed away spontaneously, and at an early period in the

course of the disease. In the female the urethral form never occurs without other portions of the genital tract becoming involved, but the converse proposition is not true; the uterus may be affected, and the most serious complications may develop in the pelvis, without the patient ever having noticed any discomfort in micturition, and without the medical practitioner who may be called in to treat the complications being able to satisfy himself that any change in the mucous membrane of the urethral meatus has occurred. As a rule the vulva becomes next affected. The nymphæ become thickened and stiff, the mucous covering becomes eroded, and the exposure of the underlying tissues thus produced gives rise to much of the suffering in micturition. At the same time the orifices of the glands of Bartholini become inflamed, and similar tissue changes take place in those about the urethral orifice. In the ordinary Bartholinitis the disease spreads inwards and the glands become painful and swollen, but if the ducts do not become obstructed the swelling subsides, and a discharge from the mouths continues for some time in much the same way as from the urethra. Although the ostium vaginæ becomes red and inflamed in an acute attack it is never so deep red as the orifices of the ducts of Bartholini's glands. In every stage of the disease the peculiar reddening, sometimes with erosion, at and near these orifices, is always distinctly visible. The reason of this appears to be that the mucous membrane about the ostium vaginæ, especially that within the remnant of the hymen, does not readily take on a diseased action; it is not a suitable soil for the development of the gonococcus. In women who are fastidious as to personal cleanliness you can hardly ever see any marked signs of vulvitis. In the careless, on the contrary, you not only find vulvitis, which may be due to the development of the gonococcus, but you find an erythema of the external surfaces of the labia and of the perineum which cannot possibly depend in any way upon the specific micro-organism of gonorrhœa, except inasmuch as the increased discharge due to the presence of the micro-organism becomes acrid and irritating, even to the external integument when left in contact with it. It stands to reason, therefore, that much of the tissue change which occurs in many cases of vulvitis depends more upon filth than upon anything specific.

It is not unusual to hear the acute form of gonorrhœa

referred to as vaginitis, by a sort of euphemism, and yet it is still a question whether there is any such thing as gonorrhœal vaginitis. The vagina seems to be the last portion of the genital tract, from the uterus downwards, to become affected, and the first to get well under any suitable cleansing process. Why should this be? Any one who has seen the uterus when a state of prolapse has been for long its usual position, cannot have failed to be impressed with the similarity of the vagina to the external integument. It has no genuine mucous membrane, merely a comparatively slight modification of the outer skin, and its surface is covered, like the outer skin, with a more or less horny epithelium. Such a surface is not easily invaded by the disease-process, and, indeed, in even well-marked cases of urethral and uterine gonorrhœa, it is sometimes hardly possible to detect any changes in the vagina. Schwarz[1] maintains that a vaginal gonorrhœa is not rare in the acute form, and he says he has seen it in cases where the uterus remained intact, and the vaginal changes could not therefore be attributed to contact of irritating discharges. But the discharge whch produces the erythema may come from outside, from beneath. If a woman is suffering from an extensive urethral and vulvar inflammation, with œdema and erosions of the nymphæ, the discharge will be copious, and flow into the vagina when she is lying in certain positions, unless the ostium vaginæ be very firm and contracted, which is not its usual state in the class of case under consideration; and in this way the infection may be set up and the symptoms increased by the production of an erythema from irritation, such as has just been alluded to as affecting the skin near the genitals under certain favoring circumstances. The younger the female affected the softer is the vaginal lining, and the more readily does a true gonorrhœal invasion result; we may therefore consistently maintain that a true gonorrhœal vulvo-vaginitis of the adult is rarely or never seen, and yet accept the evidence with regard to the specific nature of the vulvo-vaginitis of young children. Schwarz says that gonococci are to be found in and under the deeper epithelial layers of the vaginal lining, but he does not express himself so as to imply that he has found them. If, however, this turns out to be a

[1] "Die gonorrhoische Infektion beim Weibe."—*Sammlung klinischer Vorträge*, No. 279.

true observation, corroborated by capable observers, it follows that a genuine gonorrhœal vaginitis does exist.

On the other hand, and the fact may be referred to only as showing the difference of opinion which perhaps still exists, Martineau[1] does not look upon vaginitis as a directly specific disease. He describes the appearance of the vagina as seen through the speculum—the intense redness, the prominence of the plicæ, the layer of greenish pus covering the mucous surface, the small erosions, "superficial, red, and readily bleeding, which result from the desquamation of the epithelium produced by maceration in the vaginal fluid," and then he goes on to say: "I consider the vaginal granulations as an anatomical expression, as a clinical modality of the inflammation of the mucous membrane of the vagina, and not as the expression of a lesion proper to a virulent affection, blennorrhagia, or to a physiological condition, pregnancy." The vaginal granulations, according to him, merely tell us that the patient is affected with a constitutional malady or diathesis, such as the scrofulous, arthritic, or herpetic. This statement does not seem to add much to our knowledge, but clearly implies that the author, who speaks of having made observations on over 2,000 cases of blennorrhagia in women, is not satisfied with the ordinary explanation of the phenomena of the disease as it appears to affect the vagina.

Continuing the consideration of the parts affected by the acute form of the disease, we now come to examine the question of uterine gonorrhœa. The existence of a gonorrhœa of the cervix was formerly denied. Then its existence began to be recognised as possible; now, all the most recent observation goes to prove that *it is the rule, not the exception.* For my own part, I have seldom failed to demonstrate its presence by the examination of the muco-purulent discharge taken direct from the os uteri in recent cases, which were proved to be gonorrhœal by independent evidence. In uterine gonorrhœa, the mucous surface of the vaginal portion undergoes changes very similar to those referred to as affecting the inner surfaces of the nymphæ. These are reddening, swelling, and punctiform erosions. But however red this surface of the uterus may become, we can always see that the lining of the cervix is still

[1] "Leçons cliniques sur la blennorrhagie chez la femme," p. 72.

a deeper color, and that it is swollen, perhaps bulging out from the os. The inflammation spreads upwards in the cervix, giving rise to a copious purulent or muco-purulent discharge; and that it spreads to the cavity of the uterus we may infer, in the absence of direct observation, from the enlargement which takes place, and from the change in the type of menstruation, which is a uniform, or almost uniform, consequence of uterine gonorrhœa. It is this copious discharge which so frequently produces those changes in the vaginal mucous membrane over which it flows, and even in parts more external, which have been referred to as questionable evidence of a true gonorrhœal affection of those portions of the genital tract.

In describing the topography of the area of infection in a typical case of acute gonorrhœa, we might think it necessary to stop with the invasion of the cavity of the uterus. But, whether typical or not, there can be no doubt that in a very large proportion of cases the processes of the disease extend still further.

The process extends to the Fallopian tubes, ovaries, and peritoneum. Why this extension should occur in some cases and not in all, I cannot suggest any explanation further than by calling to mind what is implied in the varying vitality of the infecting organisms, and in some idiosyncrasies in the individual attacked, the consequently variable effect that might be anticipated from the varying initial force of the onset, and the nature of the soil, favoring or otherwise the development of the gonococci. In any complete investigation of this point, it would also be necessary to eliminate, as far as possible, all cases in which the gonorrhœal infection had already occurred even in an almost imperceptible "creeping" form. Between the virgin adult and the harridan subject of *colica scortorum,* there must be every shade of susceptibility. It cannot be a question of the narrowed condition of the uterine canal preventing the free flow of the discharge away from the orifice of the Fallopian tubes, for we see some of the worst results of extension of the process in women who have been recently confined, or in whom there is some subinvolution of the uterus with wide canal. Whatever be the causes of variation in the extent of invasion, we find frequently that acute gonorrhœa spreads along one or both Fallopian tubes. Here the process must destroy the ciliated epithelium, and give rise to a collec-

tion of fluid, if the canal does not remain patulous. We do not know by direct observation what goes on in the tubes, but we know that the processes of tissue reaction against the invasion of the fungus give rise to hydro and pyosalpinx, and to the permanent closure of one or both ends of the tubes; and we may suppose that occasionally the changes are so slight as to permit of resolution, and the return to a comparatively normal condition. We see something similar in the glands of Bartholini, where the disease, in an almost closed cavity, gives rise to pain and swelling, ending usually in resolution with a mild chronic disease of the part, but sometimes in complete closure of the duct, and the formation of abscess.

Whether the process of gonorrhœal disease, having once reached the tubes, ever stops short there, it is hard to say. The probability is, that it always extends more or less to the peritoneum. We know that the salpingitis causes enlargement and lengthening of the tubes. It may, therefore, produce adhesions by peritonitis originating in the extension of the disease perpendicularly through the walls of the tubes, just as peri-urethral phlegmon may result from urethritis; but it is much more likely that the peritonitis results from the continuation of the process in the same way as it has thus far extended, or by the discharge of fluid from the end of the tube. If there be a special acute gonorrhœal form of peritonitis, it spreads, as a rule, very rapidly over the pelvic peritoneum. The pain produced by the extension to the peritoneum is sometimes the first thing that attracts attention to the nature of the disease. The process has extended so far painlessly, but almost suddenly an aching begins in the pelvis, rapidly increasing to severe pain, and on an examination being made, perhaps within twenty-four hours after the first apparent symptom, the whole pelvic floor is found to be hard and immovable. In cases in which the peritonitis is set up by a sudden discharge of a coccus-containing pus or mucus from the free end of the Fallopian tube, it is conceivable that death may rapidly ensue from the shock. Noeggerath describes a case of almost sudden death from shock, which he attributes to the extension of the gonorrhœal process, but it is highly probable, nevertheless, that his patient died from perforating ulcer of the stomach. How violent the onset of the stage of peritonitis may be without any symptoms of shock is illustrated in a hospital case

under my care in August, 1887. The temperature chart is before me, and at the time the patient had to take to bed, after complaining for two days, the temperature in the axilla was 103.4°, and in the vagina 105.2°, the constitutional symptoms being in proportion to the pyrexia.

When the disease extends to the peritoneum it immediately attacks the serous covering of the ovary, and extends some way within the capsule. It gives rise by the tissue reaction to very considerable enlargement of the ovary, and, as the process of inflammation dies out, to thickening of its covering, and to more or less extensive adhesions to the neighboring viscera. How ovarian abscess may occur at a very early stage it seems by no means difficult to explain. We know that the ovaries of adult women often present considerable cysts or cavities without producing any symptoms, and while continuing to perform their functions in a perfectly physiological manner. These are the changes in the ovaries which are so often pointed to as a justification *post factum* for their removal, when no better justification is, or can be, forthcoming. Now supposing one of these cysts, with limpid contents, is situated near the surface of the ovary when the gonorrhœal process begins, its walls or a portion of them must become involved, the fluid contents increase and become turbid, and the cyst must either burst or become an abscess, just like the closed Fallopian tube, or the closed gland of Bartholini. Some such severe complications or accidents are required to explain the extreme amount of pelvic disease, and the persistency of the inflammatory processes, in a considerable proportion of cases. While the process can be observed beginning, and, as far as touch is a criterion, ending, in a few weeks in the milder cases; in the severer sort very grave symptoms are set up, and the disturbance of function, along with indications of anatomical changes, continues for months and even for years.

As bearing upon this portion of the subject, and indicating to what extent these opinions have taken hold among some clinical observers who have given the subject close and prolonged attention, I cannot do better than quote the following passages from Martineau's work: "The tubes are ordinarily affected in blennorrhagia, say the authors. They also frequently give origin to pelvi-peritonitis. Thus think Mercier,

and Bernutz and Goupil. A. Tardieu reports the case of a young girl, affected with vaginitis, who died of peritonitis. At the autopsy he found a metritis of the mucous membrane of the uterus, with suppuration; the tubes were filled with pus.

"With regard to pelvi-peritonitis, its existence is admitted by authors since the publication of the work of Bernutz and Goupil. In the sixteen months which they have devoted in this hospital to the study of this affection, there have entered ninety-three patients affected with blennorrhagia, and twenty-eight of those, that is to say, nearly a third part, presented this complication. In the tabular statement of the cases, one sees that the pelvi-peritonitis only develops when the discharge is already of long standing. These authors have never seen it produced by sympathetic action; it has appeared to them, in every case, to have been the result of the propagation by continuity of the inflammation from the vagina to the mucous membrane of the cervix, from thence to the body of the uterus, and then onward to the tubes. The morbid condition of these has become the point of departure of the pelvi-peritonitis."

It is only right to add that Martineau holds the directly opposite view from that reached by Bernutz and Goupil. He proceeds to intimate to his readers how large is the amount of material on which he bases his conclusions, and adds: "You will find by a close examination of the material that primary uterine blenorrhagia is extremely rare. In about two thousand cases I have seen it only ten times at most. You will find, further, that ovaritis and salpingitis are so rare, that I have not been able to pick out a single case. As to pelvi-peritonitis, I have found it only twice."

When opinions are so divergent as these, one, at least, of the sides to the controversy must be in the wrong. All the results of recent observation go to discredit Martineau's conclusions.

A general gonorrhœal peritonitis must be a very rare occurrence. The bowels and omentum evidently become matted together, and form a barrier beyond which the process cannot extend. It is thus confined to the pelvic peritoneum. This well-established clinical fact would seem to point to the conclusion that the extension of the inflammation is, as a rule, carried on, not by a gush of dammed-up gonorrhœal fluid from the Fallopian tube, but by some slower process, which brings the tissue reaction deliberately into play, giving time

for the raising of a barrier against the further advance of the process.

The position we have now reached, then, with regard to the acute form of gonorrhœa in women is that the ordinary typical attack extends to the cavity of the uterus. This is a position which I confidently maintain, and to the further proof of which I hope to make some contribution. Whether in the ordinary typical case the process also involves to some extent the tubes, ovaries, and pelvic peritoneum, there is still room for doubt; but I firmly believe that such an extension of the disease is by no means unusual, though it ordinarily disappears without recognition, or is attributed, without any serious effort at diagnosis, to inflammation of the bowels, or to some other cause. This class of case has been described so far as acute, but it is by no means a type of disease that runs a rapid course like the acute gonorrhœa of the male. We sometimes find that the peritoneum has been reached in a remarkably short period from the time of the patient's first contact with the infecting discharge, but as a rule the process takes from two to three months while it still may be considered in the acute stage. The external symptoms, those of the urethral or vulvar affection, have perhaps long disappeared, while the disease is still spreading on in the acute form in the uterus, tubes, or peritoneum. It may be best now, in order to support this statement with regard to the time required, to illustrate the course of the disease by mentioning the facts of two cases, which might almost be said to be taken at random, but for the selection of a case in which menstruation was suspended owing to lactation, for the sake of comparison.

Case 15.—A hospital patient seen for the first time on the 10th of June, 1887. Her only complaint was a sense of weakness, which she attributed to a very copious vaginal discharge. She was confined four months previously, she is suckling the child, and she has not menstruated since she became pregnant. Two months after her confinement she began to suffer from scalding and frequency of micturition, but not to an extent to cause much distress. Though she had passed through her confinement without any unfavorable incident, the urinary troubles were supposed to be due to after-effects of labor. On examination it was seen that there was a profuse yellow discharge staining the clothing and adhering to the pudendal

hair. There was no redness or swelling about the urethra or vulva, except an intense reddening of the orifices of the vulvo-vaginal glands. The vagina was somewhat reddened in parts, but it was not tender, for the most careful examination could be made at the first interview, and a Fergusson's speculum introduced without evoking any complaint. The discharge was found to come entirely from the os uteri. The uterus seemed somewhat tender to the touch, the mucous lining was reddened, and there was considerable erosion round the os. There was no marked enlargement of the uterus; a slight subinvolution would have accounted for the whole amount. No complication affecting the ovaries or peritoneum could be made out by examination, and the anamnesis suggested nothing of the sort. This case might have been passed over as one of slow involution, with, perhaps, some amount of endometritis from some unknown cause if the discharge had been slightly less, but for the striking appearance of the orifices of the vulvo-vaginal glands. This led to examination of the discharge, and the gonococcus was found again and again in the most characteristic form. The husband failed to respond to my request for an interview. On the 18th and 19th of June the patient complained of pain in the hypogastrium, and it continued to a slight extent until the 24th, when she was again examined. No changes could be made out in the pelvic floor or in the organs, but the pressure required for the bi-manual examination caused more pain than usual. When last seen on July 12th, after a month's treatment, the patient was considerably relieved of her discharge, but there was still a sense of discomfort in the pelvis, without any coarse change sufficient to enable me to make out thickening or enlargement. Lactation and the consequent absence of menstruation appears to have saved this patient from the usual perimetritis. In any case, such process of disease as was going on and produced the symptoms of the 18th of June, nearly three months from the onset, bore still the mark of an acute disease.

Case 16.—The husband of a lady, whom I had attended years ago in a confinement, came to me in the spring of this year (1887), and explained, with much circumlocution, why he feared that his wife had become affected with gonorrhœa. He himself was now almost well, as he had been under treatment, and the contagion must have been conveyed at the beginning

of his attack. His wife was very reticent as to her symptoms, he said, and he could give no exact details. A few days afterwards she came to consult me, and she then appeared to be very ill. I learned the following facts:—She was last confined ten months before, and the child was weaned a month ago. Her symptoms have lasted already for over three weeks, and began with scalding in micturition, but not to a severe extent, and without unusual frequency. This discomfort had passed away altogether since an abdominal pain came on four days ago. After being on her feet for two hours or more she began to have pain in the hypogastrium, and it has continued. She has resolutely gone about and attended to her duties, but has felt very languid and weak since undergoing the fatigue which was followed by the hypogastric pain. On examination, the vulva and labia were found to be smeared with purulent discharge, but without reddening or tenderness to touch. There was no sign of active disease about the urethra, but the orifices of Bartholini's glands looked *sore*, deep red, with area of lighter color extending outwards on the pale vulvar mucous membrane, and moist, as if the epithelium were eroded. The vagina was slightly reddened, but not tender, and the duck-bill speculum was used in the course of examination without causing pain. The os was open, with a considerable laceration of the cervix with red raw surfaces on the right side, and there were extensive erosions of the vaginal portion. There was a copious flow of purulent discharge from the cervix, and this was found on examination to contain gonococci in abundance. High up to the left, behind the broad ligament, an ill-defined mass, or an area of stiffened tissues, could be felt, pressure upon which caused considerable pain. The ovaries could not be made out, and no further examination was attempted. Her pulse was 126: temp. 99° in axilla. When I next saw the patient, a week later, she was just ceasing to menstruate. The flow had amounted to flooding, and she had felt ill all the time. On examination it was now found that the pelvis was full of an exudation mass of very hard elastic consistency. The difference of resistance on pressure between the two sides implied that the diseased condition affected chiefly the left side, and I have no doubt the obscure thickening which I had felt at the last examination was the beginning of the process.

Under treatment for nearly a month the patient improved,

and the mass began to feel more elastic and less hard, but she had again a flooding menstrual period, followed by an increase in the pain and the constitutional disturbance. The third menstrual period was not accompanied by any relapse. When last seen, less than a month since, she had still a profuse discharge, but the perimetritic exudation could be only obscurely felt, and there was little discomfort.

This patient had acute symptoms for certainly over two months; even though the perimetritis came on comparatively early, the chronic stage could not be said to be reached within the first three months. It may be mentioned incidentally that if this patient had become affected while suckling, and she had come under my care, I think I would have vetoed the weaning in order to save the patient from the damaging effects of menstruation, and in this way we might have succeeded in aborting the perimetritis.

In the Chronic or Creeping Form.

Coming now to the consideration of the chronic and creeping form of gonorrhœal infection in women, let us take the facts of a typical case. A young woman, a year or less after marriage, finds that her health has undergone a serious change for the worse. Whereas, before marriage, she was as sound in health and as active as in childhood, she has now lost her buoyancy, her sense of physical well-being, and is distressed by unwonted pains and discharges. She has a persistent leucorrhœal discharge; she suffers from dysmenorrhœa more or less severe, and her menstrual periods, which were formerly painless and regular in occurrence, duration, and amount, are now painful, profuse, and variable. We elicit a history of gradual change in the type of menstruation, and the slow invasion of a sense of distress of an indefinite kind, calling attention to the pelvic and abdominal regions; or there may be the history of an abortion followed by more or less severe inflammation; or the patient may have borne a child at full time, and after some form of puerperal illness, she may have experienced a persistence of pelvic troubles, with subsequent sterility. In any such case a physical examination will probably reveal certain pathological changes in the sexual organs. There is the reddening, already referred to, at the

orifices of Bartholini's glands; the uterus is somewhat enlarged to the touch, and pressure upon it causes pain, whether from its own condition or from the pressure being conducted to sensitive neighboring organs; the ovaries are enlarged, tender, and dislocated, and there is probably also a thickening and fullness about the broad ligament, implying a greater or less degree of disease of the tubes; and thoughout the whole pelvic floor there is conveyed to the muscular sense of the examining finger the impression of a deviation from health of the tissues; there is loss of elasticity in the boundary walls of the fornices, which is never felt unless the parts have been at some former time changed by an inflammatory process. Examination with the speculum shows that there is a discharge from the os uteri more profuse than normal, though it is not necessarily changed in appearance or in other characteristics; and there is probably some reddening and hypertrophy of the mucous membrane where it appears at the os.

Such are the chief points in a fairly typical case. But the symptoms and signs of the disease which I am attempting to describe vary greatly, from mere vague discomforts and slight derangement of the menstrual type to such a serious state of matters as is produced by pyosalpinx and its necessary concomitants. The symptoms and the apparent injury to health vary with the temperament and the social circumstances of the patient. If she can rest and be well attended to, there is only the inability to enjoy the more active occupations and amusements to complain of, and the injury to the general health as shown by the appearance and condition is comparatively slight. When the patient must exert herself to any considerable extent, and cannot rest even at menstrual periods, the effects of the disease are soon made evident. The superadding of nervous symptoms in long-standing cases, with perhaps no apparent relation to the original local troubles, is one of the common-place phenomena in gynæcology, and need only be mentioned.

The state of health just described is characteristic of gonorrhœal infection, and it is reached either through a more or less acute attack subsiding into the chronic form, or by the gradual development of the creeping form of gonorrhœal invasion, in which an acute stage either does not exist or altogether evades observation. How can we explain such

serious changes in the pelvic organs as we frequently find without any preceding acute attack of gonorrhœa? The answer brings us back to Noeggerath's latent gonorrhœa in the male. The virulence of the gonorrhœal infection appears to depend upon the number and the vitality of the gonococci contained in the infecting matter. In an acute attack, the number of gonococci in the secretion is at its highest, and it would seem that the micro-organisms developing in fresh and suitable soil, are in the most vigorous state of vitality; hence the infection is conveyed quickly and with certainty, and, if to a virgin soil, with the result of producing an attack of the same virulent type. At the other end of the scale you have the sort of attack produced by the infecting matter from a man who has been the subject of an acute attack many months, perhaps years, before. The gonococci are few and decrepid, probably altogether absent from the periodic emissions of a continent man. It is only the post-nuptial sexual excess that rouses them into sufficient vigor to be harmful. Even then the gonococcus, developing under a fuller blood supply and a changed innervation, but in a comparatively worn-out soil, has not sufficient vitality to gain a footing in any part of the female genital tract except the most favorable to its growth; and its *locus electus* is the cervix uteri. It would seem that it is from this point that the disease in a woman who has become affected through the "latent" gonorrhœa of her husband, almost invariably spreads upwards and downwards. The discharge produced by the tissue-reaction set up by the feebly active development of the micro-organism may carry the infection downwards, and cause some slight vulvitis, with itching or discomfort, and it is possible that in this way the urethra and the glands of Bartholini may become affected when the *materies morbi* is of medium vitality; but, as a rule, the disease spreads upwards only, and the first symptoms are those of an endometritis.

The further course of the disease is, as a rule, intermittent. Just as in the male the blood supply and innervation of repeated sexual intercourse may be required for the sufficient development of the gonococci to make them capable of fresh growth in new soil; so in the woman, the periodic blood supply of menstruation, and the *status menstruatis*, may be necessary for the further development of the disease, even when it

has taken hold. We find clinically that there are exacerbations at the menstrual periods, and we can, under favorable circumstances, trace the course of the disease as it attacks one part of the genital tract after another, each new departure appearing to be from a menstrual period. If the woman has become pregnant before the infection takes place she may go on to full time, and then it is only in the puerpery that the disease begins to spread beyond the cervix, giving rise to the gonorrhœal form of puerperal fever, and all its after consequences. If the pregnancy and the gonorrhœal infection occur in quick succession, it would seem that then the development of the micro-organism may become the cause of abortion; to the abortion succeeding the further spread of the disease, in whose course, in fact, the abortion is a mere episode.

When the gonococci have once invaded the glands of the cervix uteri, they appear to linger there as long or longer than they do about the deeper parts of the male urethra. Developing in a new soil, they are endowed with greater vitality than the comparatively starved stock from which they sprung, and therefore the woman who has become affected with even the creeping form of gonorrhœa is probably in a much more contagious state than the man from whom she contracted the disease. A very intricate case bearing upon this point will be mentioned directly.

This long-continued vitality of the gonococcus in the cervix uteri, as a cause of the spread of contagion, has been already incidentally referred to. It is a fact not sufficiently recognized by the framers of rules for the inspection of *puellæ publicæ* in some countries, and hence the whole proceeding is a delusion and a snare.

The critical reader will have observed that in speaking of the "latent" gonorrhœa of the male as the cause of the creeping form of gonorrhœa in the female, no mention has been made of the presence or absence of a urethral discharge in the infecting individual. Here there is certainly a hiatus in our knowledge. Several men whom I have had occasion to question have admitted to observing after marriage the occasional return of a discharge or a moistening of the meatus which had long disappeared; others had failed to observe anything of the sort. Careful examination by the surgeon may sometimes lead to the discovery of a pathological condition, even

when the patient quite honestly denies the existence of manifestations of it. Noeggerath, in the recent paper already quoted from (p. 22), says he has sometimes succeeded in a suspected case in bringing to light a drop of pus from the posterior portion of the urethra long after the patient believed all signs or symptoms of an attack to have disappeared. But, is a visible external discharge a necessary accompaniment of the contagious condition in the male? Probably not, and for the following reasons. The men whose wives seem never to escape are those who marry a few months after being "cured" of a gonorrhœa which has run a protracted course. These are the men who get nearly cured by several surgeons in succession; or who, after undergoing the routine medical treatment for a few weeks or months, without exercising the self-control essential to rapid and complete cure, let the affection take its course, and being no longer in pain, are satisfied if they can conceal the evidences of the disorder. Such men almost invariably become the subjects of posterior urethritis; and it is reasonable to suppose that long after the signs of active disease, including discharge, have disappeared from the anterior part of the urethra, the micro-organisms, hybernating as it were, in the posterior part of the urethra, may be roused to a point of vitality sufficient to enable them to be carried away, and to develop in a new soil, without giving rise to such local irritation in the anterior portion of the urethra as to attract attention. If we could get at all the facts of one of the mildest of cases, we should probably learn that there was some change in sensation, some slight deviation from the standard of perfect physiological action, which would point to the posterior portion of the urethra as the seat of a pathological process. The most careful examination might not lead to the detection of the gonococcus. Neisser says he has discovered it as long as three years after the acute attack, but most investigators have failed to find it a comparatively short time after the acute symptoms have disappeared. In this respect the majority of observations agree with the results of Bumm's examination of the various stages of the disease in the conjunctiva, where it was found that the gonococcus disappeared from the tissues at a certain stage of the process. The question then arises, In what form does it persist? And here again we reach the limits of our knowledge. Säuger has

suggested a spore, which has not yet been isolated, as the permanent form of the contagium in the tissues, but this is so far a mere hypothesis. The only fact which I can suggest in its favor is something which, so far, I have seen no reference to, and which may be a mere mistake in observation. In examining the discharge in a case of acute gonorrhœa with the highest powers, one is struck, not only with the vast number of diplococci, both connected with pus or epithelium and lying free, which are to be seen in the field, but also with the innumerable minute objects, call them granules or spores or *débris*, which are everywhere mixed up with the cocci. So far I have only seen this phenomenon in acute cases, and for aught that any one can as yet allege to the contrary they may be the spores of a fungus, such as we must see in tubercle were the bacilli to disintegrate and cast the spores about; and some portion of them may be destined to remain in the tissues, when the full-grown organism is cast out, until a fresh pabulum has developed or until there arrives a new stimulus to further growth.

I have repeatedly alleged that it is the neglected cases of gonorrhœa in the male—those which become chronic—which most frequently gives rise to the infection of the female, even though they may have long ceased to show signs of activity. If this statement can be proved, the fact has obviously very important bearings.

Proceeding on the plan hitherto adopted, I shall give here two specimen cases, which, of course, illustrate more points than the one at present in question.

Case 17.—Hospital patient, wife of a working man whose occupation appears to be incompatible with personal cleanliness. Her married life, except a few months at first, is a history of constant bad health. The patient is now 38 years of age, and has been married six years. She had a still-born child at the end of the first year after marriage. She was attended by a midwife, and is said to have had a "low fever" after her confinement, and was ill for two months. Never been pregnant since. She had flooding and irregular menstruation for two years after her confinement, and one of these periods was supposed to be a miscarriage, but the assertion is founded on a mere midwife's diagnosis without the patient's knowledge of facts to warrant it. Menstruation is now

scanty; period usually one day. Great pain in hypogastrium begins at periods, and is said to be worse about a week after. Profuse leucorrhœa in intervals. On examination, the vulva was found to be normal; the uterus was apparently in the normal position, and very tender to the touch, but more careful examination later showed a lateral flexion; the left ovary enlarged and sensitive, right not made out. The speculum showed the cervix slightly lacerated and flattened, with erosion round the os; a thin yellow discharge, rather profuse. These facts were elicited at the first interview twelve months ago, and on a subsequent occasion it was discovered that there was narrowing of the internal os with a chronic endometritis and sensitiveness of the uterine canal. The patient has been under treatment ever since without any appreciable improvement. She is always ailing, but not so ill as, in my judgment, to justify me in proposing removal of the diseased ovaries and tubes, especially as I infer from the thickening of tissues in the pelvic floor and the deformity of the uterus that there must be strong adhesions of long standing. Suspecting the origin of the patient's troubles, I obtained an interview with the husband. I learned from him that he contracted gonorrhœa rather more than a year before his marriage, but he was not sure about the time. The pain was not very severe, and the discharge did not trouble him, so he "took no notice of it." It was better and worse for a long time. He took his "glass of beer of a Saturday night," but would not admit to any kind of excess. He rather thought he had some of the discharge shortly before his marriage, and he may have seen it sometimes after, but he was not certain. From the wife I could obtain no evidence of any symptoms that might not have been equally due to pregnancy.

My interpretation of the facts is that the wife became affected by a low creeping form of gonorrhœa after she became pregnant, and that the disease developed rapidly into a comparatively virulent form after parturition, with the results described.

Case 18.—A lady, æt. 30, who, at the time she first came under my observation, had been married two months. Ten days after marriage she was seized with a sharp pain in the hypogastrium, and though she got up and dressed she could not walk, and had to spend some days on a couch. She and

her husband returned home, owing to her illness, and she then for the first time sought for medical assistance. The pain in the pelvis continued, and she felt so ill that she had to take to bed. She says she was treated for "inflammation of the bowels," and was under treatment four weeks, when she was considered cured. She had hardly attempted to attend to her domestic duties when the illness seems to have relapsed, but she went on for nearly a month without further treatment. It was then that I saw her for the first time. She looked very ill, and told me in answer to inquiries that she had lost flesh rapidly since the beginning of her illness. She still complained of a pain in the hypogastrium, in the groin, and round the loins. There was a profuse discharge, she said; but she used to have "the whites" before marriage, only the discharge was now much more profuse, and it was different in appearance. Since her marriage she has menstruated twice, both times very profusely, and for a longer time than formerly. On examination I found the uterus was fixed, with exudation which was most marked on the right side, but extended round behind the uterus and occupied the left half of the pelvis, where the inflammation seemed to have been less intense. It was not very tender on pressure. There was a profuse yellow discharge which bathed the external parts, but did not appear to have set up any intense inflammation about the vulva. I obtained some of the discharge for examination, and afterwards found the diplococcus in the characteristic relations, but the microscopic appearances were never those of a gonorrhœa in the acute stage.

I had an interview with the husband, and obtained from him a rather remarkable history. Seven years ago he became affected with gonorrhœa for the first time, and appeared to have had a very bad attack. He was in the hands of a quack and of several medical men in succession, and appeared to have got cured about twelve months after the first symptoms of the disease. He had been circumcised in his early youth or infancy, and there remained two sinuses in the foreskin, one of which ran parallel to the urethra, at the side of the frenum, and the other was rather more transversely placed. The former was about an inch deep, and the latter was much more shallow. Ever since the attack of gonorrhœa these sinuses had remained moist, and were sometimes irritable; he could

then squeeze out a little moisture, or a tiny drop of turbid fluid from them. Soon after his gonorrhœa was cured this man married. In the course of the first year his wife had a child, and died of puerperal fever. The child survived, and was under medical treatment from its birth; but as he himself had to be abroad on business, and, on learning about the death of his wife, remained away for several years, he could not give details concerning this period.

He never saw any sign of urethral gleet since his final cure before his first marriage, but about twelve months ago, owing to the irritation caused by the deeper sinus, he consulted a surgeon, who slit open and cauterised the canal. The smaller one was let alone.

Both husband and wife were perfectly well to all appearance at the time of the marriage, two months ago, and the illness from which the wife is suffering came on without any apparent cause. But since her illness the husband has begun to suffer from urethritis. It came on four weeks after marriage, and at the time of my first interview with him it had developed, though under treatment, into a rather acute urethritis, and it ran the course of a moderately severe attack of gonorrhœa. As he had been under treatment for three weeks or more, I was not surprised at being unable to detect gonococci in the discharge, and I entirely failed to discover any suspicious micro-organism in the minute speck of fluid which he could press from the orifice of the small sinus.

The question arises then, Whence came the infection to the woman? Of course, some accidental contact with a gonorrhœal poison is a possible explanation, but it is a marvellous coincidence that a woman of thirty should have escaped so long only to become accidentally infected at a time when the infection would be conveyed to her husband. From my knowledge of the facts, I would say that the suspicion that this respectable woman of thirty contracted a disease from another source just on the eve of her marriage may be peremptorily set aside. Besides, the infection did not act like ordinary acute gonorrhœa. In the woman the perimetritis came on as soon as the discharge, and the discharge did not readily infect the husband, unless the husband is simply lying. We seem almost driven to the conclusion, therefore, that the gonorrhœal virus lingered in the sinus for years, only to

develop actively when it reached the favorable soil of the uterine canal, and that it spread in the manner characteristic of "latent" gonorrhœa, but with exceptional rapidity.

The wife, who was kept under constant treatment for over three months more, considered herself well at the end of that time, but though the uterus was then movable, the thickening of the peritoneum was distinct. There was the peculiar loss of elasticity all across the pelvic floor, and the deep-lying sense of resistance. Probably both tubes were ruined, the fimbriæ matted together, or adherent to the ovary, and the abdominal orifices closed. There may be now no further complication; a sort of resolution has apparently gone on, and the patient may escape any of the more serious injuries to her health. But menstruation, which continued to be still too profuse, will never again be perfectly normal, and the closing of the Fallopian tubes can never be undone.

CHAPTER V.

CONSEQUENCES OF GONORRHŒAL INFECTION TO THE INDIVIDUAL.

In discussing the consequences which may, and most frequently do, arise from gonorrhœal infection in women, I shall not attempt to place the pathological changes in one series of paragraphs and the immediate and remote effects of these changes on the individual in another series, but mention them together, and that as concisely as possible. This method of treating the subject seems to possess some advantages, although to a certain extent it involves repetition.

Urethral and Vulvar Gonorrhœa.

The urethral form of the disease is exactly analogous to the same disease in the male, and lays the subject of it open to nearly all the same complications. From gonorrhœa in the female may result cystitis, disease of the ureters, and of the kidneys, just as is the by no means rare consequence in the male.

Chronic inflammation of the glands of Bartholini is almost too trivial an ailment for mention in the present relationship. Acute inflammation may be a very painful ailment, and when the disease has spread onwards this painful affection may be a somewhat serious hindrance to effective treatment. In a case which came under my care in October, 1887, the right gland developed so rapidly into an abscess that it was impossible to carry out the proper treatment for preventing uterine blennorrhœa until the Bartholinitis was thoroughly dealt with. This required chloroform narcosis and the use of the cautery, and then measures could be taken which prevented the further spread of the disorder. In only one case (which has been mentioned) have I been able to convince myself that

chronic Bartholinitis was more than an inconvenience—viz., that in which a pessary, when it slipped a little, seemed so to press upon the tender spots corresponding to the site of the glands, as to add very considerably to the patient's sufferings.

Uterine Gonorrhœa.

The invasion of the cervical canal is marked by the appearance of a profuse mattery discharge. It would appear that a rapid change takes place in the epithelium both of the cervix and of the cavity of the uterus. The cylindrical epithelium is destroyed for the time being, and is probably never perfectly restored. Its place is taken, to some extent, by layers of a sort of pavement epithelium, in fact, a kind of cicatricial tissue. There thus occurs a deeper change than that which takes place at the menstrual period, profoundly modifying the fresh developments of the mucous membrane for the future. Without going into detail, these are the results obtained by Zeller[1] in his investigation into the subject of endometritis, and they are just the changes which we might expect from what we learn from Bumm's inquiry into the action of the gonococcus in the conjunctiva. The results obtained by Mr. J. Bland Sutton, in a recent investigation into menstruation in the human female and in monkeys, bring home to us more clearly the cause of a most important sign of gonorrhœal invasion of the body of the uterus. His conclusions are: 1. The uterine mucous membrane is normally not shed during menstruation, but only the epithelium. 2. The sanguineous discharge is due partly to oozing from the surface denuded of epithelium, and in part to active congestion. 3. The discharge from the uterus is largely augmented by mucus secreted in increased quantity at this period from the enlarged utricular glands.[2] Keeping this in mind as the physiological process, we can well understand that the superadding of the tissue reaction produced by the gonococcus would at first merely exaggerate the amount of menstrual flow, whatever the remoter effects might be. The pain and nervous derangements which ultimately super-

[1] "Plattenepithel im uterus (Psoriasis uterina)."—*Zeitschrift für Geburtshilfe und Gynäkologie*, Bd. IX., Hft. 1. Summary in *Centralblatt für Gynäkologie*, No. 10, 1885.

[2] *British Gynæcological Journal*, Part VIII., Nov., 1886.

vene are probably due to changes in the tubes and ovaries as well. To the later changes in the lining of the uterus, when it assumes its almost cicatricial character, are probably also due the remoter changes in the menstrual discharge, which, instead of being profuse as at first, becomes scanty in amount and sometimes changed in character. In addition to the endometritis there comes on a greater or less amount of hyperplasia of the uterus, and with this there must necessarily be some derangement of innervation. The sense of dragging and sacralgia in the early stages is not probably from mere weight alone.

The increased menstrual flow is such a constant feature in uterine gonorrhœa, that I shall introduce here two typical cases. In one of them it was the sudden change in menstruation, without apparent cause, in an unmarried woman, which excited suspicion and led to a correct diagnosis.

Case 19.—P. B., æt. 23, single, domestic servant, residing in Preston, sent to me by her mistress on November 9th, 1887. She was suffering from pain in the hypogastrium, supposed to be the result of a kick from a refractory child. There was a history of good health up to six weeks since, when her symptoms began. She had a rather sudden attack of severe pelvic pain four weeks ago. Her last menstruation was unusually profuse and continued for a fortnight. Since then there have been mattery discharge, hypogastric pain, etc. My diagnosis, after examination, was gonorrhœal endometritis, salpingitis, ovaritis, and perimetritis of the left side; and I elicited information from the patient which proved the diagnosis correct. She felt very ill, and I advised her to seek admission into Preston Infirmary, under the care of my friend Dr. Garner, to whom I wrote. She was accordingly admitted on Nov. 17th. Dr. Garner has kindly sent me the notes of the case, from which I select the points relevant to my present purpose. The patient was under treatment till the 13th of January, when she was dismissed cured. She was kept rigidly to the recumbent posture, and suitable measures were taken to diminish the congestion of the pelvic organs. Three days after admission the vaginal temperature became normal. She began to menstruate on Nov. 28th, and continued till Dec. 7th, extract of hydrastis having been administered from the 5th, owing to the excessive hæmorrhage. The general and local treatment

was continued until the 1st of January, when she began to menstruate again with much less pain. The period lasted only till the 5th. Examination on the 11th of January showed an entire absence of pain on pressure, though there was still considerable thickening of the tissues in the left half of the pelvis. The uterus, which had been fixed, had begun to recover its mobility.

Case 20.—R. N., æt. 21, single, living at home with her parents, who are of the respectable working class, applied for treatment at the Manchester Southern Hospital, on February 10th, this year (1888). After hearing several irrelevant and misleading statements as to the patient's past and present state of health, and the treatment she had undergone, I learned that she had had a profuse and prolonged menstrual period, without any apparent cause, at or about Christmas. This fact led to some pointed inquiries and a thorough examination, about which the condition of the pudenda indicated there need be no scruples, the result being the establishment of the diagnosis of perimetritis with salpingitis of both sides. The patient, after admitting certain facts, answered questions frankly enough, and finally the following points were settled: —(1) Scalding in micturition began four months ago; (2) the first profuse menstruation occurred at Christmas, and the last period, which ended a week before the date of our interview, was also extremely profuse; (3) the hypogastric pain began at the time of the profuse period at Christmas; (4) she felt so ill again, just after the last period, that she had to take to bed, and she had got up, the first time for a week, to come to the hospital. The cause of the increased pain and feeling of illness was no doubt a menstrual exacerbation in the perimetritis. But the sudden, apparently causeless, increase in the menstrual flow is the chief feature of the case, as an illustration of the point under consideration.

Tubal Gonorrhœa.

But by far the most important changes in the internal sexual organs which result from the gonorrhœal infection are those affecting the Fallopian tubes and ovaries. With regard to the tubes, it would seem that the effects vary greatly, according to the virulence of the infection. If the virus is in a state

of high vitality, the disease may spread so rapidly along the tubes that the abdominal ends become sealed by the peritonitis before the active stage of tissue reaction has ceased in the course of the tubes. The consequence is that the tube becomes distended by the collection of fluid that forms, thickened in its walls, and perhaps lengthened as well. We thus reach the condition of hydrosalpinx, which will, under favoring circumstances, sooner or later, advance to the still more serious condition of pyosalpinx. When the process of invasion of the infection is slow, as in the creeping form, we very seldom see it resulting in pyosalpinx. Yet there can be little doubt that many of the cases of puerperal pyosalpinx are the result of the assumption of a comparatively virulent type under favorable circumstances by a chronic or creeping gonorrhœa. Pyosalpinx is certainly not a rare consequence of gonorrhœal infection, and it does more serious injury to health and is more dangerous to life than any of the other complications. Yet the risk which the affected run of having their health ruined and their lives endangered by this condition is by no means even yet generally recognized and acted on by the medical profession in this country. As far as I can learn from the literature of the subject, Mr. Lawson Tait is the only English surgeon who has continued for years to call attention to this complication. He has taken occasion to refer to gonorrhœa, again and again, as the cause of the severer forms of Fallopian disease in cases where he found operation necessary, and even in his work on "Diseases of Women," published in 1877, frequent reference is made to gonorrhœal infection as a factor in the production of some of the more serious complications. He says,[1] in reference to ovaritis, "Acute ovaritis from gonorrhœa is a common result of the infection, and is a frequent cause of sterility. . . This affection, as far as is known, generally results in disorganisation of the gland and the formation of adhesions round it." He also recognises gonorrhœal infection as one of the most ordinary causes of perimetritis. In the edition of his work on diseases of the ovaries, published in 1883, he says:—"I have already said enough about hydrosalpinx and pyosalpinx to render it quite unnecessary to discuss them further than to insert here a complete list of all the cases upon which I have operated for these diseases. Both conditions are far more common than was believed previous

to my experience, yet they have been quite well known, and described for at least half a century. Of the forty-four cases only four have occurred in single women, and the leading feature in the history of many of the cases was an attack of gonorrhœa. In one case I had to operate in the acute stage of the disease, which had arisen, on the admission of the husband, from this cause."[1]

At a meeting of the Obstetrical Society of London, held on the 4th of May last, when Dr. A. H. N. Lewers read a paper founded on observations made on the pelvic organs, in a series of 100 cases, in the post-mortem room of the London Hospital, the essayist reported that disease of the Fallopian tubes—that is, pyosalpinx, hæmatosalpinx and hydrosalpinx—was found in seventeen cases, and he read notes descriptive of these. Dr. Galabin, in the course of the discussion on the paper, mentioned that at Guy's Hospital the pathologists had found in 302 necropsies of women only twelve cases of distension of tubes, and two of these were very trivial, amounting in all to a proportion of 4 per cent. The cases of chronic inflammatory disease about the tubes amounted to 9 per cent. Mr. Lawson Tait spoke in eulogy of Dr. Lewers's paper. He found the conclusions drawn from the post-mortem room, as regards causation, progress, prognosis, and treatment, identical with those which he had been preaching for about ten years on the basis of clinical experience. He confessed that it was somewhat a staggering thing to find 17 per cent. of the women who died in the London Hospital suffering from tubal disease, and this did not include those cases which suffered the most, in which there were adhesions between the ovaries and tubes to the surrounding viscera, more particularly the peritoneal layer lining Douglas's pouch, resulting ultimately in complete retroversion of the uterus with its appendages, and forming one of the most dreadful conditions which the gynæcologist had to deal with. When removed it was difficult for an unskilled pathologist to see anything the matter with them. Dr. Lewers had not included such cases, and they must have been numerous. *He thought the explanation of the higher percentage at the London Hospital, and the small group*

[1] "The Pathology and Treatment of Diseases of the Ovaries." 4th Edition, 1883.

at Guy's, must be due to locality, and that gonorrhœa was more common amongst the poor at the East End than on the south side of the river.[1] I do not know if the speaker gave reasons for this final remark, but, to those who have no local knowledge, it may be as well to explain that the London Hospital contains, in the area from which it chiefly draws its patients, the localities where sailors most do congregate, and among the women who apply for its relief are the victims of the neglected venereal diseases brought into a focus from every sea-board slum in the world. The same state of matters prevails in such places as Liverpool and New York, and we have perhaps in this fact alone some explanation of the frequent occurrence of the more serious forms of tubal and ovarian disease in these cities.

In Germany, the man who has, perhaps, most persistently called attention to the more serious clinical features of the gonorrhœal infection in women, is Sänger, of Leipsic. His views may be concisely and conveniently indicated by a quotation from a recent paper read before the Chicago Gynæcological Society.[2] He says: "Salpingitis gonorrhoica is the only specific infectious form of salpingitis which is recognised as such by Lawson Tait, although he stops short of admitting that the gonococcus is the exciting agent. Without doubt the gonorrhœal is the form most frequently met with. This fact was clinically established as early as 1872, by Noeggerath, long before Neisser had discovered his gonococci, or Lawson Tait had performed his first operation 'for suppuration of the uterine appendages.' In Germany, I myself was one of the first gynæcologists who at our meetings showed the frequency of gonorrhœal salpingitis, emphasised its causal connection with pelvic peritonitis, and removed by operation the gravely implicated uterine adnexa. Gonorrhœal salpingitis is never followed by a 'destructive suppuration' of the uterine appendages; it remains invariably a disease of the surfaces of the mucous and serous membranes. The pus formed by the specifically diseased mucous membrane gradually distends

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[1] "Summary in the *British Gynæcological Journal*, Part X. (August, 1887), p. 273.

[2] "Salpingitis gonorrhoica et syphilitica."—*The Obstetric Gazette*, February, 1887.

the tube; in one class of cases, in which there is a great accumulation of free pus, the tube is transformed into a large sac with thin walls; in another, in which the wall of the tube, especially its muscular tissue, is hypertrophied to a greater extent, the tube becomes much thickened and rigid. In most cases both conditions are found, the uterine portion of the tube is thickened, the abdominal end dilated. The serous surface of the tubes, the albuginea of the ovaries, the serosa of the peritoneum are attacked or become pus-secreting surfaces only in cases in which gonorrhœal pus has escaped from the tubes and thus infected the above-named structures. . . . I do not believe that gonorrhœal pus ever penetrates the walls of the tubes and thus produces these diseases. But a specific gonorrhœal inflammation of the mucous membrane of the tube, with secretion of pus into the cavity of the latter, is accompanied by a non-specific inflammation of the entire tubal wall."

My present object is only to call attention to the most advanced opinion at home and abroad on the spread of gonorrhœal infection to the Fallopian tubes, and the consequences which result therefrom; it is not to assist in attracting attention to this polemic, much less to seek to take part in it. But if the illustrative case of pyosalpinx, which I am about to mention, does not also amount to a case of "destructive suppuration of the uterine appendages," it would be hard to describe the state of matters in English.

Case 21.—Mrs. B., the wife of a well-to-do operative in a Lancashire town, is 34 years of age; has been married seven years, and has never been pregnant. She has always suffered from dysmenorrhœa since puberty, and this continued unchanged after marriage. Her husband contracted gonorrhœa six months ago, and at once infected his wife. Both husband and wife were under the care of the same practitioner, their family doctor, at the same time, the wife being ignorant of the nature of her ailment. She had a very severe acute attack, and about six weeks after the first symptoms, she completely broke down at a menstrual period, and had to take to bed. She was in a state of fever, and complained of intense pain in the pelvis, chiefly affecting the left side, and extending upwards towards the crest of the ilium, and down the thigh. The doctor found the uterus fixed, and the pelvic floor hard, rigid, and still painful. She was under treatment at home for four

months, during which time she was chiefly confined to bed; she lost flesh, had night sweats to slight extent, and suffered almost constant severe pain in the pelvis, with nocturnal exacerbations. When she first came under my care, five months from the time of the infection, she was still in the condition just described. The uterus did not seem much enlarged, and the exudation appeared to be most marked on the left side of the pelvis. The chief pain was still in the left half of the pelvis. The profuse yellow discharge, which was said to have existed at one stage of the disorder, had almost completely disappeared. The patient was treated with glycerine and iodine tampons, and hot-water douches, as well as medicinally. She was unable to be out of bed for even a very short time. She menstruated twice while under observation, each time with intense pain—an exaggerated form of the ordinary pain—accompanied with vomiting, excitement, and sleeplessness. After persevering for six weeks with this treatment, I could observe no improvement except that the exudation in the pelvis began to permit more movement of the floor, and a tumor could be less indistinctly made out about the left broad ligament. This I concluded was formed by a Fallopian tube distended with pus. During the six weeks of treatment the patient menstruated twice, each time with the greatest disturbance to the ordinary state of health, including increased pain, vomiting, and headache. Instead of going home to resume an invalid life, the patient resolved, after consultation with her friends, to submit to operation, which was proposed to her. At the operation I found the omentum adherent to the bladder, so that it had to be ligatured and divided before I could reach the tumor. It was then discovered that the uterus was like a small projection in front of and between two bulging tumors which filled up the greater part of the pelvis. With great difficulty the adhesions of the tumor on the left side were partly broken down, and while I was working at the lowest and posterior part of the mass, trying to make a sort of pedicle, the cyst burst and filled the field of operation with a flood of stinking pus and venous blood. The cyst was got away, and after repeated irrigation, sponge-packing, and finally the application of perchloride of iron, the hæmorrhage was arrested, but this was done only after considerable loss of blood, much exposure of the parts,

and the loss of much time. The cyst on the right side was larger and not so tense, and as it was clear that the patient could not stand a repetition of the proceedings, I resolved to stitch it into the abdominal wound. This was partly done, and the tumor was then cut open. Its contents were also offensive pus, which was got away by sponging and irrigation. The pelvic cavity and the whole field of operation were carefully cleaned by irrigation with saline solution. The pelvis was drained with a Kœberlé's tube, and the cyst with a rubber tube, and then the wound was closed. The patient seemed at death's door for about thirty hours. She then began to revive. When she was apparently out of danger, she complained of an intense pain in the pelvis after a violent attack of coughing, and she sank rapidly and died. Examination of the wound showed that the stitched-in Fallopian tube had given way to a slight extent, but sufficiently to permit the entrance of the antiseptic fluid used in dressing into the pelvic cavity. In this case the left cyst was an abscess of the ovary, and the Fallopian tube enlarged, hard, and sinuous, could be felt firmly tied down in front of it, as it were, along the top of the broad ligament. The tube was let alone, as I have repeatedly seen perfect restoration to health in cases requiring abdominal section where such adherent non-distended tubes were not interfered with.[1] The cyst on the right was the Fallopian tube.

As far as the patient was concerned, we had here a frightful state of matters produced by a virulent attack of gonorrhœa, the relation of cause and effect being clear and unequivocal.

Pathologically, was it not a case of suppurative destruction of the appendages? the ovary a mere abscess, the other tube, from one end to the other, an abscess, and the corresponding ovary buried beneath it. The thick-walled cyst is in my possession. Must I look upon it as a sort of sandwich consisting of two layers of specifically inflamed tissue, a mucous and a serous, holding between them a layer of non-specifically inflamed muscular tissue, as Sänger appears to allege? If so, what is the theoretic or practical value of such a view?

Anticipating here a point with regard to treatment, I cannot help thinking, from my experience of many similar cases, that is, of abscess of tube or of ovary *adherent to the pelvic floor,*

[1] See *Medical Chronicle*, November, 1887, and January, 1888.

that the best treatment is by operation from the vagina, instead of by abdominal section and the breaking down of the barriers raised by nature against the further invasion of the peritoneum by the process of inflammation. I have had several cases within the last two years which show in a striking manner the efficacy and safety of vaginal incision with drainage.

Effects upon the Ovaries.

Continuing the consideration of the anatomical changes which produce the clinical signs and symptoms of gonorrhœa, we now come to the spread of the infection to the ovaries.

We have seen that great changes may be produced upon the tissues of the Fallopian tubes, resulting in the closure of the ends of their canals and the formation of hydro and pyosalpinx. The fimbriæ not only become matted together by the inflammatory process, but they frequently become attached to the surfaces of the ovaries, and the parts become so modified by the disease in the course of months and years that when they are removed by operation, for the relief of the sufferings caused by the anatomical changes and interference with function, it may be impossible to identify in detail the parts belonging respectively to tube and to ovary. If the disease reaches the fimbriæ, it almost certainly goes on to produce perimetritis and ovaritis. There is no leap from one point to another; the susceptible tissues are continuous. It is the custom to speak of an interval between the ends of the tubes and the ovaries, and to speak of the acute affections of the tissues of the intervening space as peri-oöphoritis. Anatomically there is an interspace; physiologically there is none; and clinically there is no distinct form of disease arising from the inflammation of the particular portion of the peritoneum about the ovary. There is no peri-oöphoritis without inflammation of the ovary itself, and more or less extensive perimetritis; and the symptoms arising from this extension of the inflammation are the symptoms due to inflammation of the pelvic peritoneum and of the ovary. Olshausen, who devotes part of a chapter to peri-oöphoritis, finishes his remarks by admitting that no such disease is distinguishable from pelvic peritonitis. He says: "The symptoms of this peri-oöphoritis differ in no

respect from those of a circumscribed peritonitis. . . . What I have here called peri-oöphoritis may be, in the majority of cases, just as well designated perimetritis."[1] It is, in fact, not in the majority of cases, but in all, just the inflammation of the peritoneum within the area that the ovaries can reach in their physiological movements, and it is, therefore, the inflammation on which the adhesions ultimately formed by the ovaries depend. This fact, perhaps, justifies a distinct name.

Resisting the temptation to paraphrase the usual writing of the text-books on the inflammation of the ovaries, what I have to say on the effects of gonorrhœa upon these organs, whether correct or not, I can concisely state. The inflammation is for the most part superficial. It is a peritonitis rather than a process affecting the substance of the ovary, but that it also not infrequently is a parenchymatous inflammation is proved by the symptoms, by the acute enlargement of the ovary, and by the remote effects. The symptoms of the first acute attack may include the peculiar pain like that with which we are familiar in cases of orchitis, and we may be able, either before the peritoneum has lost its limpness or after the perimetritis, when its subsidence is rapid, to make out the enlarged ovary as an element in the case, but I question very much if this is not the exception. In some severe cases the parenchyma is certainly involved, and the process goes on rapidly to the formation of abscess; but there is then, as has already been remarked, probably some favoring circumstance, such as the pre-existence of some cystic degeneration in a part of the ovary. A case which may be referred to in illustration of this point was mentioned by Dr. Lewers, at a meeting of the Obstetrical Society on January 4th, 1888.[2] It was that of a woman who was admitted into the London Hospital suffering from parametritis a few days after her confinement. She died, and on post-mortem examination it was found that the right ovary was greatly enlarged, "it was adherent to the adjacent surface of the broad ligament by recent lymph, and on section an abscess containing half a drachm of pus was found." The broad ligament itself was as yet only in a state of phlegmon. Thus the ovarian abscess was premature; it

[1] "Die Krankheiten der Ovarien," Stuttgart, 1877.

[2] *British Medical Journal*, January 14th, 1888, p. 78.

was in advance of the general process of inflammation. Probably there was a small pre-existing cyst.

The enlargement which we find later in the history of a case is a secondary result, as I shall try to show. By the peritonitis which attacks the covering of the ovary, that covering, the tunica albuginea, is permanently injured. The acute inflammatory state, here or elsewhere, is followed by one of two results: the surface becomes adherent to another surface, or, remaining free, it becomes entirely changed in character—a sort of cicatricial tissue, thickened, toughened, and devoid of its columnar epithelium. There can be little doubt that in every case there is an exudation from the inflamed surfaces, and if this fluid could be imagined, in the severer attacks, as drying up, like the sap of some plants after injury, that is to say, becoming organized into a tough pseudo-membrane, embracing ovaries, tubes, and uterus, we would seem to have an explanation of a not uncommon effect. In some of the cases which we operate upon we may have diagnosed enlargement of the ovaries, dilatation of the tubes, or some other condition accompanied with symptoms which justify surgical interference. On making an abdominal incision we find that by reason of this membranous product of inflammation the examining finger seems to be almost as far from the affected organ as it was in exploring per vaginam. Now the difference between such an extreme case and the mildest, as far as the changes in the tissues are concerned, is one of degree. After an attack of medium severity the ovary becomes in part adherent, and in part the surface is thickened, or covered with a membrane different altogether in character from its original tunica albuginea. The most important consequence of this change appears to be that although the ovarian stroma is little affected, and the Graafian follicles mature as usual, they do not burst externally to the ovary. Where the surface of the ovary is adherent to the bowel, or uterus, or broad ligament, or pelvic peritoneum, the follicles cannot burst; this is obvious enough. But where the surface of the ovary is apparently free they do not burst. A crisis comes in the development of the follicle, and a change takes place in it, but that which would have been a corpus luteum under normal conditions will be found after the same lapse of time a mere apopletic cyst. Such cysts grow. How they

increase I do not know; perhaps by affording a more favorable surface for other follicles to burst through; perhaps by hæmorrhages during subsequent menstrual periods. I have many a time seen such cysts the size of a pigeon's egg, and once or twice even as large as a hen's egg. I do not say that in all these cases the origin of the disease was gonorrhœal, but in all there were signs of old peritonitis, with thickening of the covering of the ovary, and with an entire absence of the signs of recent ovulation near the surface. When this thickening of the covering of the ovary occurs, we can see how certain it is to be accompanied with clinical signs. When the periodic congestion returns, the organ cannot expand as it does under purely physiological conditions. What part of the pain is caused by a sensitive organ pulling upon the adhesions, it is not possible to say, unless the same cause be proved to act, and its amount be ascertained, in the intervals; but that most of the pain is caused by the compression exercised by an unyielding capsule there can be little doubt. The first sufferings caused by the acute onset are those of an attack of peritonitis; they can be relieved, and will subside; but the pain produced at a later period by the efforts of the ovary to expand, or relieve itself from adhesions, is an ever-recurring form of suffering. It may bring on a variety of secondary symptoms, or become so urgent, merely as pain, that operative treatment may be the only mode of giving relief. When the process of disease has reached this stage, the danger to life may be unimportant, but the misery produced by the pain and disturbance of function may be intolerable.

Abscess of the ovary is not one of the common results of gonorrhœa, but that it may occur as the direct consequence of infection there can be no doubt; and it is therefore to be kept in mind as one of the complications by which an attack of gonorrhœa in the woman may lead to a fatal result. Having occurred, it is about as dangerous as pyosalpinx, but it is by no means such an ordinary result of the disease. The great majority of cases of abscess of the ovary are puerperal, or they arise in apparently healthy girls from sudden suppression of the menses, or they occur in scrofulous and tubercular subjects. Gonorrhœa probably results in abscess only in very violent attacks, or when some pre-existing pathological state of the ovary, such as a cyst near the surface, is favorable to

its development. To what extent there is a "mixed infection" when acute ovarian abscess occurs, we have as yet not sufficient clinical material for forming a judgment.

The possibility of an ovary or tube become cystic in the way I have just described, by a unilateral attack of perimetritis, permitting impregnation to occur by means of the healthy side, and ultimately becoming the seat of fatal puerperal septic abscess, has been suggested in a recent paper by Dr. Grigg.[1] The four cases described formed nearly the whole of the mortality of Queen Charlotte's Lying-in Hospital in one year; the patients were all unmarried women of questionable antecedents; and careful post-mortem examination in every case showed that the fatal result was owing to old inflammatory disease of the pelvic viscera, very suggestive of the changes produced by gonorrhœal infection. But for the post-mortem examinations the cases would have been, in all probability, set down as simple puerperal sepsis originating at the time of parturition.

Sterility a Consequence of Gonorrhœal Infection.

We speak of the physical suffering resulting to women from the gonorrhœal infection under various names, implying greater or less structural changes in the internal sexual organs. We say one suffers from leucorrhœa, another from dysmenorrhœa depending upon changes in the position of the uterus, contraction of the canal of the uterus, disease of the tubes and ovaries, or some other cause; another is menorrhagic, and another shows symptoms of one of the more serious affections of the tubes or ovaries, and so on. But, perhaps, the most important consequence may be summed up in the word *sterility*. This is by far the most common result of one or other of the anatomical changes produced by the gonorrhœal infection. *A woman who has suffered from gonorrhœal perimetritis is barren.* Sterility is the result of one or more of the anatomical changes which have been referred to, and co-exists with one or more of the groups of symptoms which we designate by various names, as if they

[1] "On the Dangers arising from Diseases of the Uterine Appendages in Childbed." *British Gynæcological Journal*, Part VII., November, 1886.

were distinct diseases. It is easy to see how the inflammatory process, resulting from the gonorrhœal infection, should have sterility as one of its consequences, whatever other clinical signs or symptoms of disease might be produced. My belief is that perimetritis of both sides most necessarily be followed by sterility. In this condition we see the possibility of fruitful intercourse being attacked and destroyed; the ova are hindered from even leaving the organ which is their source, and, consequently, their impregnation by the male element becomes an impossibility. Even in cases which do not extend to perimetritis, we can conceive that the condition of the Fallopian tubes might be rendered such as to make sterility an infallible result. The tubes become sealed at either end as the direct consequence of the inflammatory process, and even when the canal remains pervious the lining epithelium must be so injured or destroyed that the passage of the ovum is prevented. In such cases of comparatively slight damage, there is danger of the congress of ovum and sperm resulting in tubal pregnancy, or some other form of ectopic gestation.

Should the ova escape from the ovaries, and the tubes remain pervious, there are still the changes in the uterine lining, and in the calibre of the canal, to interfere with the normal course of the impregnation and the development of the ovum in utero. The secretion from the uterine mucous membrane may be so changed as to act as a poison to the ovum, on its arrival in the uterus; but it must be confessed that this condition is more likely to result from a syphilitic taint than from gonorrhœa. The mucous membrane of the uterus may be in such a condition that every attempt at nidification is rendered abortive, or as a somewhat later consequence, stenosis of some part of the canal may occur and interfere mechanically with the passage of the spermatozoa. The usual seat of contraction is the internal os. I am quite well aware that there is a fashion with some therapeutic nihilists among the gynæcologists of sneering at the mention of mechanical obstruction to the passage of spermatozoa as a possible cause of sterility. Being microscopic objects, to them a needle's eye would be a wide thoroughfare. That is clear enough as a question of proportion between the size of the spermatozoon and the diameter of the eye of a needle, but there must be something more in the question than a simple arithmetical

relation. From the nihilists we have not yet obtained a rational explanation of the cases in which dilatation of the uterine canal is directly followed by conception, after years of barren conjugal life. Even if it be alleged that there is a dammed up and changed secretion in the uterine cavity which is the direct cause of separating ovum and living sperm, still the stenosis is the cause of the retention of discharge, and therefore the cause of the sterility.

The stenosis may be secondary, and come on long after sterility has been established by gonorrhœal perimetritis. I have under treatment at the present time a woman of twenty, who has been married two and a half years. There is a clear history of gonorrhœal infection during the first year of married life, and when she came under my care, for the first time, a year ago, there could still be made out some thickening in the perimetrium. There was also a profuse uterine discharge, but the gonococcus could not be detected in it. Since then well-marked stricture of the internal os has come on, with intense dysmenorrhœa of the mimic labor type. A long probe, with a head about half the size of that of the ordinary sound, passes with some hesitation, causing a distinct type of pain, which the patient says is similar to that which precedes and accompanies the menstrual flow. I do not doubt but that this patient will at some future time, in some other hands, be confidently treated for simple stenosis, for the relief of dysmenorrhœa and sterility. The pain may be then relieved, as it will now be by me; the dysmenorrhœa may be temporarily cured, but the sterility never.

The sterility which results from gonorrhœal infection may be produced by the first acts in consummating marriage, as in Case 2, page 271; or pregnancy may occur and end in abortion produced by gonorrhœal disease of the uterine mucous membrane, as in Case 9, page 277; or pregnancy may go on to full term, and be followed by a gonorrhœal puerperal illness with perimetritis. This perimetritis then produces the anatomical changes on which life-long sterility depends. An example of this class, one-child sterility, we have in Case 3, page 272. Whether abortion is ever produced by a gonorrhœal disease of the fœtal or maternal coverings of the ovum cannot be as yet said to be proved, but there is ground for a strong presumption in favor of the existence of a gonorrhœal abortion, and a

sterility post abortum gonorrhoicum. The sterility produced by disease developing in the woman directly after marriage is a familiar and common occurrence. Every practitioner of experience must be able to call to memory cases of the kind, and those who have not been disposed to give to gonorrhœa its just share of the blame, will find, if they carefully investigate the possible causes of sterility in women who were apparently robust at marriage, that the more closely the subject is examined the greater are the dimensions which gonorrhœa assumes as a factor in the production of sterility in the female.

Gonorrhœa is also the cause of sterility in the male in some unknown proportion. Gross inquired into the facts of 192 cases of sterile marriage, and found that the male was the cause in 33 cases, or 17 per cent. of the whole, and that azoospermia existed in 31 of the 33.[1] Kehrer's cases, which are included in these figures, gave 14 in 40 of male sterility, all owing to azoospermia, and in the majority gonorrhœa was shown to be the original cause of the pathological condition. Sänger states that he has found one-third of all sterile marriages to be owing to azoospermia in the male, the result of gonorrhœa. "If we consider, in addition to this, the cases in which sterility is caused by gonorrhœal disease in the woman, the man retaining his potency, we find that gonorrhœal infection takes the first place in the etiology of female barrenness, and is of far more importance than all the other causes put together."[2]

While on the subject of sterility, I have only to add that cases are not unknown in which the gonorrhœal infection sets up perimetritis, and yet the inflammation remains entirely confined to one side. We have an illustration of this in Case 13, p. 303, quoted from Dr. Angus Macdonald's paper. In such cases the women may go on bearing children, just as women do with one ovary removed, as after ovariotomy; but such cases are rare. It is but seldom that the inflammatory process produced by the spread of the micro-organisms remains circumscribed. Either as the result of a continuous process of

[1] J. Matthews Duncan, *Gulstonian Lectures*, 1883.

[2] "Ueber die Beziehungen der gonorrhoischen Erkrankungen zu Puerperalerkrankungen."—*Verhandh. d. deutschen Gesellschaft für Gynäkologie*, Leipzig, 1886.

development the disease reaches the other side of the pelvis, or there is a sudden invasion at some of the early menstrual periods after the infection. A perfect example of this class of case is mentioned in Mr. Lawson Tait's "Diseases of Women" (p. 211).

Case 22.—"Some years ago a gentleman, who had been a short time married, visited a neighborhood where he unfortunately met a friend of his bachelor days. Within 48 hours he came to me in terrible distress, with the initial symptoms of gonorrhœa, but with the still more terrible dread that he might have conveyed it to his wife, for intercourse had taken place a few hours before his symptoms appeared. Of course, I at once cautioned him to refrain absolutely from intercourse with his wife, advice which I have no reason to believe he disregarded. His gonorrhœa proved very trifling, and passed off entirely in less than a week. Wishing to take his annual holiday he brought his wife to me to make sure that she was free from disease, and I could not find the slightest trace of vaginitis. I therefore sanctioned their travelling to a considerable distance. But within three days I was summoned to her, and found her suffering from a most severe attack of inflammation of the left ovary. After some weeks she got well, though the ovary could be felt, both by rectum and vagina, as large as a small orange, firmly fixed and exquisitely tender. Suddenly the right ovary became similarly affected, and after a most severe illness, during which she seemed frequently at the point of death, she recovered, with the right ovary similarly large and fixed. She never menstruated after this second illness, and she now lives a semi-invalid life, hardly ever free from pain, and unfit for any great exertion, though, as time goes on, her sufferings seem to obtain slight amelioration. She is quite unable to endure marital intercourse."

Whatever exceptional cases we may meet with of women bearing children after an unequivocal attack with pelvic gonorrhœal complications, still we may hold firmly, for all practical purposes, to this conclusion, that *the woman who has suffered from gonorrhœal perimetritis is barren.*

Gonorrhœal Puerperal Fever.

As to the extent to which gonorrhœal puerperal affections occur there is a great difference of opinion, partly because

there is a want of sufficient observed facts to compel unanimity. Sterility after one pregnancy, whether ending in abortion or full-time parturition, is a fact of frequent occurrence. In all such cases efficient observation would have revealed the presence of puerperal inflammation of the uterus or adnexa, or both. The question is, in what proportion of the cases is the gonorrhœal infection the efficient cause of the barrenness, and in what proportion does the condition depend upon a puerperal septic inflammation? Sänger professes to have already succeeded, by some process of clinical observation, apart from investigation for the presence of micro-organisms, in differentiating the gonorrhœal from the other cases. He has found a type of puerperal fever in which the symptoms come on late in the puerperium. This is his gonorrhœal form; and he maintains that it occurs frequently in women who have been infected with gonorrhœa. "In the gonorrhœal post-partum affection it is the salpingitis which secondarily produces the affection of the pelvic peritoneum, and it does so with a frequency which does not occur in puerperal infection, and also in the pre-antiseptic period could not have occurred. The septic-puerperal salpingitis to which Buhl, E. Martin, Spiegelberg, and others attached so much weight in the causation of puerperal peritonitis, is met with almost exclusively only on the post-mortem table. The gonorrhœal tubal disease of lying-in women leads, perhaps, never to a fatal end, and, after the resorption of the accompanying pelveo-peritonitic exudation, it can usually be readily made out by the bi-manual examination. From this it follows that if there is present a disease of the tube, of the uterine appendages, of the pelvic peritoneum after confinement or abortion, there is reason to suspect a gonorrhœal origin to the ailment. I have been able to find among 230 cases of gonorrhœal infection 35 cases, equal to 15 per cent., in which the gonorrhœal affection of the uterine adnexa and of the pelvic peritoneum could be referred back to the puerperal state, and in the majority of these cases the acute symptoms appeared for the first time six or eight weeks post partum or post abortum."

Sänger may be right in his observations and conclusions. From the present state of our knowledge of the subject, I suppose no one is in a position to assert dogmatically that he is wrong—altogether wrong. I can only say that his state-

ments do not agree with anything I have observed or anywhere read; and there seems to be nothing in the nature of the case to require the symptoms in the puerperal gonorrhœal infection to be always late in showing themselves. We know that in ordinary non-puerperal cases the spread of the infection is often very rapid, and it is hard to believe that a coarse process of washing away by the lochia is one which would greatly retard the development of the micro-organisms in an otherwise favorable soil. So confident is Sänger in the position he takes up that he goes the length of referring to Angus Macdonald's cases in order to say that the diagnosis was wrong. They were, it seems, not cases of gonorrhœal, but of septic puerperal infection. It is an easy method of supporting a theory; still the conclusion, if true, would have to be accepted. The argument would, however, have been weightier if the author had seen his way to attacking the observations and conclusions of some of his living German contemporaries, who would have been obliged to reply. As the matter stands no reply is possible except from the candid reader; and whoever will take the trouble to refer to the cases (*Edinburgh Medical Journal*, June, 1873) cannot fail to be impressed with the clearness with which the sequence of events is stated, or to be convinced that the diagnosis, made by the experienced and scientific physician who knew all the facts, was in every case correct.

Kroner, of Breslau, has also investigated the relations of gonorrhœal infection to puerperal fever, and reached conclusions widely different from those of Sänger. He made a careful examination of women who had borne children that became affected with blennorrhœa of the conjunctiva, showing the presence of gonorrhœa in the puerperium. He found that 75 out of 82 mothers of children affected with ophthalmia neonatorum passed through a normal puerperal state both early and late. Only one woman, who became affected fourteen days post partum with a severe form of septicæmia, died in childbed, and her illness had no causal relation to the gonorrhœa. Two had a tedious illness beginning with fever soon after the confinement, and only four had any special troubles in the later period of the puerperium. Examination of these revealed the existence of para and perimetric "cica-

trices." Thus Kroner found a comparatively rare concurrence of gonorrhœa and puerperal illness.[1]

In a paper more recently published[2] he maintains that he has obtained still more evidence in support of his original position, and gives details.

I have purposely noticed this subject at a length somewhat out of proportion to the rest of my essay, although it is still almost purely controversial matter, because it seems to me to be a new and important subject for further observation. My own notes bearing on this question must be reserved for the present; they are as yet too few and inconclusive. I am, however, disposed to agree with Noeggerath that most of the cases of salpingitis, which we have been accustomed to look upon of puerperal septic origin, must be classified as gonorrhœal. A peculiarity of this form of so-called puerperal fever is that the patients recover very slowly, and a large percentage of them remain invalided for years, because of pelvic adhesions and deformities, whereas women who have survived an attack of genuine puerperal sepsis or sapræmia pass with comparative rapidity into robust health.[3] There is, unfortunately, too much of a polemical element in the German contributions on this question. It suggests rival schools rather than earnest laborious research with scientific truth only in view. Independent unemotional observation towards the elucidation of the points yet in obscurity is a desideratum.

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[1] "Ueber den Sitz der gonorrhoischen Infection beim Weibe." von Dr. Steinschneider in Franzensbad.—*Berliner klin. Wochenschrift*, April 25, 1887.

[2] "Ueber die Beziehungen der Gonorrhœ zu den Generationsvorgängen."—*Archiv für Gynäkologie*, Bd. XXXI., Hft. 2.

[3] "Ueber latente und chronische Gonorrhœ beim weiblichen Geschlecht."—*Deutsche med. Wochenschrift*, December 8th, 1887.

CHAPTER VI.

TREATMENT, PROPHYLAXIS, AND CONCLUSION.

TREATMENT.

THE treatment of gonorrhœal disease in women may seem, in view of all that has been said, a rather large and complicated subject for exposition. But if we set aside mere theoretical details, and deal with that which concerns only cases met with in practice, the varieties of treatment that can be reasonably employed shrink into comparative insignificance. As a specific disease there is, as a rule, little or no scope for treatment of it in the female; we have only the opportunity of trying to minimise the consequences.

Gonorrhœa as a local disorder requires topical treatment; as a specific disease, depending for its development and symptoms upon the growth of a micro-organism, it requires for its topical treatment the employment of a germicide, one or other of the antiseptic and astringent class of chemicals, which are known to destroy the ordinary micro-organisms.

In women the urethra and bladder become affected as in men, and the disease may spread from thence to the ureters and kidneys. The treatment of this phase of the disease must be practically the same as in men. Now it has been quite recently proved again by an efficient observer that the balsam of copaiva is about the best internal remedy. It was found by Dr. Oscar Oppenheimer, of Heidelberg, that applied directly to the micro-organisms it had little effect, but the urine of a person who had taken the balsam internally acted as a poison to the bacteria.

Oppenheimer[1] experimented with a large number of substances, testing the antimycotic power of the individual

[1] "Untersuchungen über den Gonococcus (Neisser)."—*Archiv für Gynäkologie*, Bd. XXV., Hft. 1.

chemical or drug by cultivation experiments with the coccus-containing matter. Perhaps the most important result of his laborious investigation is that already mentioned with regard to the effect of the decomposition products of copaiva balsam.

Professor Isidor Neumann, of Vienna, has recently published in the *Wiener med. Blätter* some chapters of a forthcoming work on the venereal diseases, and there he calls attention to the danger of kidney disease involved in an attack of gonorrhœa. Now if the danger of kidney disease be as urgent as Neumann asserts, and if Oppenheimer's observations and conclusions are correct, then the rational treatment of urethral and cystic gonorrhœa in the female, as in the male, would be to keep the urine impregnated with the balsam, or that which results from passing it through the body, so that it might act as a germicide, and prevent the invasion of a vital organ by the micro-organisms. It is surprising in the face of these observations to find Dr. Fritz Levy,[1] of Copenhagen, objecting to the use of copaiva in the treatment of women, apparently on the trifling ground that it may cause gastric derangement or a cutaneous eruption.

Along with a suitable internal medicinal treatment there can be little doubt that the best local treatment is antiseptic, and there is a consensus of opinion in favor of the sublimate, although it has disappointed expectation to some extent. Dr. Ulisse Malusardi[2] has lately published a paper, in which he passes in review the history of the therapeutics of gonorrhœa in England, France, and Germany, and gives the results of his own observations and experiments; and he concludes that the sublimate is the most efficient and safest of the antiseptics, while in the later stages of topical treatment the sulphate of zinc may most advantageously be combined with the sublimate.

These facts chiefly bear upon the urethral form, but they may also apply to the treatment of that phase of the disease which we now come to consider, viz., the vulvar and vaginal stages of gonorrhœa in the female. Here I must confess that to me it is a matter of almost purely theoretic speculation. I have seldom seen a case of gonorrhœa in a woman in which

[1] "Om den 'latente' Gonorre hos Kvinden."—*Hospitals-Tidende*, Jan. 19, 1887.

[2] "Studio etiologico e terapeutico sulla blenorragia."—*Gazetta medica di Roma*, May, 1887.

the disease had not already reached the uterus, and I am disposed to think that this has not arisen from want of clinical experience, but from the nature of the facts. We are called upon to treat only the advanced stages. One would expect an opportunity of averting the disease under the circumstances of Case 16 (p. 346), for example; but the opportunity is almost invariably denied. The guilty husband hopes for the best; and believing that if only he can deny and conceal, the wife, even though affected, cannot suffer much harm, and can never be quite sure of the facts, whatever her suspicions may be, he always puts off taking the steps which would procure suitable treatment until some serious symptoms set in. I do not know what may be the experience of those who officially examine professional prostitutes, but I believe decent women in this country who become the subjects of gonorrhœal contagion seldom or never obtain suitable treatment in time. What then are we called upon to treat? Let us take two examples in cases which have come under my notice within the last few months, in order to fix attention upon this point and once more upon the cruelty and ignorance of the gonorrhœic seducer:—

Case 23.—Quite recently I saw, in consultation with a gentleman practising in one of our suburbs, a delicate young lady who was about to be married, but had been compelled, unfortunately, to give up her preparations for marriage, and take to bed on account of some serious illness, supposed by herself and friends to be "inflammation of the bowels." At the time I saw her she had been almost entirely confined to bed for several weeks. Her female relations knew that the illness seemed to begin with profuse and prolonged menstruation, and this surprised them very much, as their young friend had, as a rule, menstruated in a slightly irregular and scanty fashion. The doctor in attendance told me, before visiting the patient, about the state of matters in the pelvis, whose existence we verified together. The patient was feverish, and appeared to be ill. On examination we found that there was an entire absence of the usual signs of virginity; the uterus was large and fixed. There was a great mass of exudation on the right side, some exudation behind filling up Douglas's space, and an indefinite fullness, without so much hardness, on the left side. This state of matters led me to inspect the

vulva, and I found the orifices of the ducts from the glands of Bartholini highly inflamed, and distinctly tender to touch as compared with the surrounding mucous membrane. The discharge from the genital tract was profuse and yellow. My colleague and I were agreed as to the anatomical condition: the only question was as to the origin of the disease, because of its bearing on the prognosis. I expressed to my colleague the belief that the disease was gonorrhœal, and I then learned that such was his suspicion. He had cautiously enquired into the matter, and ascertained that the man whom he most naturally suspected was at the very time confined to bed with some ailment, supposed to be cystitis. Although I could not obtain a satisfactory sample of the discharge for microscopic examination, I do not think there can be any doubt about the diagnosis; the clinical features and collateral facts are quite sufficient. With regard to this case it should be noted that the disease had spread to the perimetrium before medical advice was sought, probably without any consciousness as to cause and effect on the part of the patient, and that among people who would not for a moment hesitate to obtain any medical aid that might seem to them needful. If they do these things in the green tree, what shall be done in the dry?

Case 24.—A. B., æt. 25, single, dressmaker, a respectable-looking modest young woman, from a small country town, seeks advice on account of intense dysmenorrhœa, which unfits her for work for two or more days every month. It affects chiefly the left side, but for over twelve months it has been gradually growing worse on the right side, which is now nearly as bad as the original seat of pain. From the anamnesis I learned that until two years and a half ago she was a strong healthy girl, who never had a day's illness. Menstruation used to come on from puberty until then with absolute freedom from pain. She then began to menstruate profusely and somewhat irregularly. She had a leucorrhœal discharge, and commenced to suffer at the periods. For a long time the pain was confined almost entirely to the left side of the pelvis, and it came on the day before the flow, and continued to be very severe during the first two days of the menstrual period. Since the first change in menstruation the periods have continued to be profuse, lasting five or six days. The inter-menstrual leucorrhœa has ceased. On making a vaginal examina-

tion of this patient, I found, as I expected, an absence of the hymen and loss of tonicity in the vagina. The uterus was small, with a slight retroversion: the right side of the pelvis was apparently normal to touch, but somewhat tender on deep pressure; the left side was occupied by a hard firm band, evidently an adhesion from old perimetritis; there was pain on pressure upwards in the region of the ovary, but the bowels were so loaded that during this, the only examination, it was not possible to define the position and relations of the parts. The orifices of Bartholini's glands were bright red and sore-looking, while the surrounding mucous membrane was rather anæmic. I told this patient without further parley that two years and a half ago she became affected with the poison of a contagious disease, and was proceeding to give my reasons, when she interrupted me, and asked if she might explain; and then she told her story. About three years ago she was "keeping company" with a young man to whom she expected to be married. His occupation required him to be absent for several months in a large town named, and soon after his return the patient began to have certain symptoms which she described. On telling her young man of her condition he admitted that he had been suffering from a certain disorder, and he appears to have given her the benefit of his experience in treating herself. From her description of her symptoms she went through a mild attack of gonorrhœa, including perimetritis, but she never once consulted a doctor. She solemnly assured me she had lived a perfectly chaste life since her paramour left her, and when she consulted me about the dysmenorrhœa she had no idea that her present symptoms and her former illness were in any way related.

These are by no means extreme cases of gonorrhœal infection in women as it presents itself to the doctor for treatment. But the treatment of such cases is no more treatment of gonorrhœa than the performance of a plastic operation on a contracted cicatrix is the treatment of a burn. We are not treating the venereal disease, and, in private practice, we seldom or never get an opportunity of doing so.

However, if we should meet with cases in the early stage, before the uterus is invaded, we must be prepared to act energetically, and the question arises as to what is best to be done. When men become more impressed with the serious

nature of the disease, it will probably be the rule to see cases in the early stage. Schwarz,[1] of Halle, who speaks so as to give the impression of having had a large experience of purely vulvo-vaginal gonorrhœa, describes his method of treatment in the following terms: "First of all the vulva and vagina are thoroughly cleansed of the adhering secretion by means of a 1:1,000 sublimate solution; then, with the help of a Simon's speculum, the vagina and vulva, including every fold and recess, are energetically swabbed with a dossil of cotton-wool soaked in a one per cent. solution of the sublimate, and rubbed with it for several minutes, so that the superficial sheaths of the epithelium containing the gonococci are removed. The Simon's speculum, or some other with separable blades (such as Bozeman's, &c.), is essential for the purpose in view; by this means it is possible to distend the folds of the vagina to their utmost extent, and to obtain a complete controlling view of the whole process, so as to avoid missing any of the diseased patches. Special care is taken with the introitus, which contains numerous folds.

"The next step is copiously to dust over the vagina and vulva with iodoform, which is still more effectively applied by rubbing it into the mucous membrane with the tip of the finger.

"To complete the process, the vagina is with moderate firmness packed full of iodoform gauze.

"If the treatment is very painful, a thing which depends upon the intensity of the disease process, and the idiosyncrasy of the patient, a narcotic or anæsthetic must be administered.

"The process is of value only when thoroughly carried out, but then it is certain to succeed.

"If, as is usual in rubbing the vagina, there occurs extensive capillary hæmorrhage, it is only a favorable sign, inasmuch as it shows that at the bleeding points the diseased epithelial covering is for the most part removed, and, at the same time, a large number of the superficial, perhaps diseased, capillaries are destroyed.

"The iodoform gauze is permitted to remain for three or four days, and then the whole process is repeated with the same thoroughness, and over the same area.

"After four or five days more the gauze is finally removed,

[1] *Loc. cit.*

and then, for eight to fourteen days, the patient carries out a copious irrigation of the vagina with a sublimate solution of 1 in 2,000."

This process, he says, is hardly ever known to fail. The vagina is red and raw after the second tampon has been removed, and there is usually a copious purulent discharge, "but the gonococci are annihilated, and have for ever vanished."

Schwarz goes on to recommend the use of iodoform to the vulva, in order to eradicate the disease from Bartholini's glands, and he further employs compresses soaked in warm sublimate solution with the same object.

In estimating the value of this treatment, however, it may be as well to recollect that Malusardi's experiments tend to discredit iodoform as a germicide for the gonococcus; and Schwarz is still a believer in a gonorrhœa of the vagina, a phase of the disease whose existence has been rendered still more problematical by some recently published observations[1] made by Dr. Steinschneider, in Neisser's Clinic at Breslau.

The chief objection to Schwarz's method is, however, not so much its inefficiency as its severity. It is clearly unsuitable for even hospital practice in England, and, however efficient it may have proved, it must give way to some milder method.

Fritsch, of Breslau,[2] strongly recommends a solution of chloride of zinc instead of the sublimate. He says he has obtained "quite surprisingly good results." He prescribes a solution of equal parts of water and chloride of zinc. Of this solution about five drams are added to a quart of water. This fluid is warmed and used by means of the syringe twice a day, not leaving off during menstruation. If the simple syringing fails to cure he applies a stronger solution of the zinc chloride to the internal surface of the uterus, and then introduces a pencil of iodoform.

Perhaps a large part of the disappointment with the sublimate, of which so much was expected, arises from an inefficient manner of using it. It partially fails in the gonorrhœa of the male urethra, because it has to be merely injected, and probably forms on the surface of the mucous membrane an albuminate which actually protects the deeper-seated gonococci

[1] *Berliner klinische Wochenschrift*, April 25, 1887.

[2] "Notiz betreffend die Behandlung der gonorrhoischen Vaginitis und Endometritis."—*Centralblatt für Gynäkologie*, No. 30, 1887.

from harm. In the female genital tract, on the other hand, it can be rubbed in, and if the new pathology of gonorrhœa be correct, it ought never to fail.

As to the treatment of the disease after it has reached the uterus, I can speak with confidence. In order to be effective treatment must be energetic and immediate. If we have fair grounds for believing, from the absence of thickening of tissues, or of pain on either side of the uterus, that the disease has not reached the tubes, we may still hope to prevent the worst complication of all. Nothing should be done that could increase the congestion of the uterus and interfere in any way with the uterine canal until the moment the germicide is to be applied. Therefore we cannot stop to dilate with tents; the interference and delay would be fatal to success. Only once, when the hollow sound would not pass, I have rapidly dilated, wounding the mucous membrane, before applying the germicide; and this is an undesirable incident, although it does not necessarily do harm. My routine treatment has been to steady the uterus by holding its anterior lip with a vulsellum, after exposing it well with a duck-bill speculum, and to introduce the full length of the canal a Fritsch-Bozeman sound. The sound is kept in a hot disinfectant, and at the last moment the air in it is expelled and replaced by the ordinary tincture of iodine, which is injected from an ordinary two-ounce glass syringe, connected with the sound by indiarubber tubing. When the sound is in position in the uterus the tincture is slowly injected as long as it continues to flow from the opening in the outer tube of the instrument. It is almost always necessary, however, to withdraw it, in order to clear it of coagulated blood and mucus before we can efficiently complete the application; and this is a serious defect in an otherwise satisfactory instrument. The vagina can be protected from the action of the returning fluid either by rapid and frequent changes of pledgets of cotton-wool, or by constant irrigation by gravitation with warm water.

A strip of lint wrung out of sublimate solution is left in the vagina for two or three hours to give the patient a rest, and then a copious vaginal douche with a weak sublimate solution is used, and this is repeated before the next intra-uterine application. The applications should be repeated three days in succession, if no symptoms arise. The Fritsch-Bozeman

sound is laid aside for several days after the third application, and the vaginal irrigation is continued, careful note being taken of both the axillary and vaginal temperature. When the eschar or iodised uterine lining has had time to break down and get more or less expelled, the process is repeated. So far, I have seen no harm come of the intra-uterine applications, and I am confident that the proceeding has saved several patients from the further spread of the disease. Tincture of iodine is so far the only fluid I have employed. Perhaps a spirituous solution of corrosive sublimate might be used with advantage.

Schwarz employs, at the stage of the disease under consideration, a process of constant irrigation of the whole uterine canal with carbolic acid or corrosive sublimate solution. He mentions some details of three cases in which this method was most successful. The irrigation is carried on for from two to four days through a modified Fritsch's sound, and the return fluid is collected and drained away by means of a special apparatus.

Dr. Fritz Levy, in the paper already referred to, speaks of curetting the uterine canal "without previous dilatation," before applying tincture of iodine or other germicide solution. The treatment seems irrational and barbarous. No good can come of cutting up the endometrium with a curette, which, if so small as to pass the internal os without dilatation, cannot possibly bring away the bacterium-containing débris of mucous membrane which its employment produces. You cannot in this coarse mechanical way get nearer to the gonococci, and you can only succeed in choking up the catheter used to inject the germicide fluid, while laying the tissues open to the further ravages of the disease.

So much, then, must serve here as suggestions for the treatment of the uterine stage. I must confess that the opportunities which have presented themselves to me have been too few for trying variations in treatment. In the vast majority of the cases which I have seen the disease had already spread beyond the uterus by the time the patient applied for advice.

When the disease has advanced beyond the reach of topical treatment, it must be dealt with on a totally different plan. The treatment cannot now be too cautious. Nothing should be done that could possibly increase the blood-supply to the

internal sexual organs, and special care should be taken when the menstrual periods are impending. It should be remembered that some pathological conditions of the ovary may already exist which may greatly exaggerate the effects of the infection. The patient's sexual health is almost certainly about to be ruined, but her life is also in danger. If the ovaries are healthy and the tubes do not become sealed, this danger to life is comparatively slight. If even a small amount of fluid has collected in the tubes it appears to have a tendency to change into pus; and, if the fimbriated end of the tube has not become firmly sealed, undue manipulations setting up strong peristaltic action may produce rupture, followed by a fierce conflagration over the pelvic peritoneum. Such an inflammation, when set up by a fluid resulting from mixed infection, would probably not become rapidly circumscribed, but might be the origin of a general peritonitis.

It is usually necessary to keep down the vaginitis by a *warm* douche, and this is really all the local treatment which appears to be called for beyond poulticing in the acute stage of the perimetritis. The warm water, medicated or plain, may have some soothing effect; the *hot* douche may be injurious. In one of my early cases, which ended fatally (Case 6, page 274), I have always blamed the hot douche for again lighting up the inflammatory process. In order to prevent the uterine discharge from keeping up the disease in the lower portion of the genital tract, I direct the patient, even in the later stages, to use a lotion made by means of tablets of corrosive sublimate and ammonium chloride.[1] Each tablet contains two grains of the sublimate, so that when one of them is broken and thrown into a pint of warm water, the resulting solution is practically the strength of 1 in 5,000. A solution prepared in the same way should also be employed in the earlier stages of the disease, concomitantly with the intra-uterine applications. This treatment is continued until the dangers of the acute and subacute stages are over, and it is time to endeavor by suitable measures to remove the resulting exudation, to break down adhesions, and to prevent deformities.

The remoter stages of the disease, those of complications and consequences, must be looked upon as a separate chapter

[1] These tablets are prepared by Messrs. Wright and Barnaby, chemists, Oxford Road, Manchester.

in gynæcology, apart, to a large extent, from their primary cause. Gonorrhœa in a woman, when it has once passed beyond the uterus, is an incurable disease. Such an outrage as the invasion of the Fallopian tubes by a pathogenic organism Nature never forgives. Just as a burn inflicted on a child that falls in the fire is followed by a deforming cicatrix, the effects of which may be ultimately more or less relieved by surgical measures; so the consequences of gonorrhœal invasion of the tubes and peritoneum are adhesions and deformities which cannot be cured, but whose miserable consequences may be sometimes palliated by operative gynæcology.

Prophylaxis.

When we come to consider the prevention of the disease under discussion, we are met by the question: What is the legitimate function of medicine in relation to the venereal disorders? It cannot be to make vice and excess safe and easy. Medicine is not called upon to become "Procuress to the Lords of Hell." How far it may be legitimately requested to give instruction in prophylaxis, with a view to stamping out the maladies, is a question in ethics for which, fortunately, I am not called upon to offer a solution.

One relevant question, a portion of the subject, presents itself and cannot be thrust aside; and regarding it the reader, who has not given it special attention, may justly claim from the essayist, who has had the temerity to take up the subject, some suggestion, the fruit of his presumed special thought and experience. The question is: How are women to be protected from the consequences of their husband's pre-nuptial or post-nuptial vice and folly? I fear no concise and adequate answer is forthcoming. One of our greatest living philosophers has well said that the abrogation of the sexual relation would eliminate most of the poetry from human life. The destruction of that relation in the individual case, and the substitution of loathing disgust, and physical suffering, at the moment when aspirations, unconsciously the outcome of sexual vigor, which lend poetry and dignity to existence, and make men and women something more than mere mammals, are in process of reaching fruition, is a result peculiarly repulsive,

and productive of resentment against its causes. And we naturally ask: How can the sum of human misery, resulting from this special cause, be diminished? Can the women protect themselves or through their guardians? The less that women know of these matters, and are capable of suspecting, the better for society; and we can hardly conceive of a state of society in which this evil received so much attention that the guardians of young and innocent women usually inquired as jealously into certain details in the antecedents and present physical condition of suitors as they are wont to do now into their worldly circumstances.

Can we expect anything from legislation? Hardly. We have probably gone as far in that direction already as a healthy public sentiment could permit. Some of our legislation has been useless or worse, and has had to be repealed; and while recent legislation for the protection of young women may do good, if the laws be calmly and justly administered, it does not to any considerable extent reach the causes of the suffering with which we are at present concerned. If legislation could do something for the protection of young and thoughtless lads, thrown upon their own resources in our great cities, against the harridans who lie in wait for them, and in modern times perform the functions attributed to the fabled harpies, there might be some diminution in the amount of contagion afloat; but we need not look for such legislation. Men must protect themselves: they must avoid the evil or take the consequences. If the consequences were confined to themselves, nothing more need be said. But the innocent suffer most. Gonorrhœa in the woman is as ruinous as syphilis; there is little to choose betwixt the diseases. The men must protect the women. The great majority of them are amenable to reason, and would listen to the dictates of humanity and of honor if their consciences were appealed to. With regard to their wives, there is also the sentiment of self-interest to influence their actions. It only needs definite knowledge to be diffused among them as to the risk of inflicting untold suffering upon those whom they wish to protect, to greatly influence their conduct; and the only guardians of the necessary knowledge are the medical profession. While the doctors look upon gonorrhœa in women as a mere bagatelle, what can be expected of their self-indulgent male clients? As long as the medical

practitioner believes that he can produce a "precious result" at a critical time with a little nitrate of silver solution, the education of the layman will not begin; he will not be adequately impressed with the physical grounds for exercising self-control in order to escape infection, or for the need of persevering industry and self-denial in order to completely and rapidly eradicate the disorder once contracted.

The attentive reader of the notes of cases given in the foregoing pages will have observed that the worst results followed to the women whose husbands had been the victims of gleet or neglected gonorrhœa even long before marriage. The practical lesson from this observation is obvious enough: (1) Measures should be taken to have the disease cured as quickly as possible on symptoms beginning to appear; and (2) when a chronic disorder has become established it should be a positive bar to marriage until there is sufficient proof that it has been cured for many months.

And what is the criterion of cure? The question is perhaps as difficult to answer as the analogous question with regard to syphilis. We have seen that in some cases, where serious consequences to the woman followed soon after marriage, a slight urethral discharge or moisture reappearing in the male owing to post-nuptial sexual indulgence. Taking a hint from this fact, we may find a criterion of cure in some cases. The local effects of sexual excess may be sufficiently reproduced, in a given case of suspicion, by the injection into the urethra of a nitrate of silver or corrosive sublimate solution, so as to irritate and produce a slight urethral discharge, in the same way as a conjunctival discharge is produced by Credé's method of preventing ophthalmia neonatorum. The urethral discharge resulting should be carefully and repeatedly examined for the gonococcus, and a negative result would afford a strong presumption of cure. The slight sacrifice of comfort thus made by the patient would be too trifling to be considered when the importance of the result was kept in mind. This is far from a perfect method of gaining definite information, but as a criterion of cure it is better than nothing at all.

Sound judgment is hard; and it may be that in writing this essay I am joining the band of those who exaggerate the im-

portance of the form of venereal disorder under discussion, or at least see too much in recent observations and experiments. That such observations and experiments must be continued and greatly extended, sifted, discussed, and subjected to the most rigorous logical processes before we can fill up *lacunæ* in our knowledge, reconcile differences of opinion, and "in its season bring the law," I willingly admit; meanwhile we have learned enough for that practical application of our knowledge which in its turn becomes a method of research and an agent of progress. In putting this subject before the readers of my essay, I do not think I in any way exaggerate; I believe rather that in attempting to depict the fruits of our newer knowledge I use but feeble colors. I believe that the gynæcologist who fails to closely examine into this subject, repulsive though it may be apart from its scientific interest, must constantly fail in his duty to his patients; and I am convinced that when the general practitioner, to whom the domestic *arcana* are an open book, comes sufficiently to observe the phases, and duly to appreciate the import, of a large class of ailments with which he is constantly called upon to deal, the view which I expressed in the commencement of this essay will become the generally accepted opinion of the medical profession, viz., that the gonorrhœal infection in women gives rise to a group of diseases which, by reason of their clinical interest and their social and moral consequences, surpass in importance every other class of affections which claim the attention of the gynæcologist.

ON GIDDINESS.

FROM A SERIES OF

Clinical Lectures on Important Symptoms.

BY

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ON GIDDINESS.

LECTURE I.

Gentlemen: We have frequently met with giddiness as a prominent symptom in cases which we have studied in the wards, and I promised that I would take an opportunity of discussing the subject in the lecture-room, illustrating my observations by cases which I might be able to show you or describe. I find it useful, sometimes, to take up a symptom in this way rather than to discuss individual cases or groups of cases, as we usually do in this lecture-room.

Giddiness is a sensation with which we are all familiar, but which it is difficult to describe. Its essential feature is the feeling of uncertainty of our position in space relatively to surrounding objects. Sometimes one feels as if objects were whirling round more or less rapidly; sometimes one seems to be moving in the midst of them; and that apparent movement may be round a vertical or a horizontal axis, to one side or other, forwards or backwards; or there may be a sensation of sinking downwards; or the movement may appear confused or irregular. It may also be slow or rapid.

Giddiness is often associated with other disorders of sensation, such as nausea, deafness, tinnitus aurium, or other subjective sounds, dimness or other changes of vision, faintness, palpitation, hallucinations, and is sometimes followed by loss of consciousness. But it is constantly associated with impairment of equilibriation. This is readily explained when we consider that it is the result of derangement of a function essentially related to equilibriation,—disturbance of equilibriation being, so to speak, the motor aspect of the sensation of giddiness. For equilibriation we require the co-ordinated

action of many groups of muscles. This co-ordination is, like others, guided by sensory impressions, and these impressions are derived from different sources.

Neither the power of equilibriation, nor the power of appreciating the impressions by which it is guided, is inborn in man. Each is gradually developed by processes of education. The senses which are trained to subserve it are touch, sight, the muscular sense, probably an articular sense, and a visceral sense, along with the great organ of special sense for equilibriation—the semi-circular canals. Of some of the impressions we are conscious, of others not. Of sight and touch impressions we habitually take cognizance, or at least we may do so; of the other kinds of impressions we make use without any act of intellectual perception. It is at once apparent how sight subserves the purposes of equilibriation, and it becomes especially noticeable when the other sources of sensory impressions are impaired. You have often seen this in cases of locomotor ataxia. You have noticed how helpless the patient becomes when his eyes are closed. The importance of touch, and particularly plantar touch, is equally familiar to you, being often illustrated in the same class of cases. The impairment of the muscular sense, I have sometimes shown you, is at least as important as those already mentioned. The articular and the visceral are less obvious, but I think are real. I shall not dwell upon them, but the special sense for equilibriation, which has its seat in the semi-circular canals, requires fuller notice.

Let me remind you of some anatomical facts and physiological explanations. The canals are situated in the petrous portion of the temporal bone. They are three in number, and communicate by means of five openings with the vestibule. Each canal has a dilated or ampullary end, and each by its ampullary end opens into the vestibule, while two of them have their non-ampullary ends united, and communicate with the vestibule by a common opening. These canals occupy different planes, and are known as superior, posterior, and horizontal, according to their position. Within the bony labyrinth there is a membranous labyrinth, the membranes being much smaller than the canal, except at the ampullary ends. Between the bony canal and the membranes is the perilymph, with connective tissue, blood-vessels, and nerves. Within the membranous canal is the endolymph. A branch

of the portio mollis of the seventh nerve is distributed to a crescent-shaped ridge near the middle of each ampulla. The terminal nerve-structures are hair-like cells, which project into the endolymph, and which must obviously be affected by changes in it. Through the chain of bones the labyrinth is connected with the tympanum. The handle of the malleus is fixed into the tympanum, while its head articulates with the incus. The latter, again, is connected with the stapes as well as with the posterior wall of the tympanum. The stapes is fixed into the fenestra ovalis, and by its movements produces alterations in the state of the fluids in the whole labyrinth.

In 1828, Flourens discovered that the semi-circular canals have something to do with the maintenance of the equilibrium of the body. He found by experiment that section of a membranous canal was always followed by movements of the head, or even of the body, rotating about an axis at right angles to the plane of the divided canal. On section of the horizontal canals, the animal moved its head rapidly from side to side and tended to spin round on a vertical axis. When the posterior canals were cut, rapid movements backwards and forwards took place, and the animal showed a proclivity to turn somersaults, from before backwards. When the superior vertical canals were cut, similar movements occurred; but the tendency now was to turn somersaults from behind forwards. Section of all the canals induced peculiar irregular movements. The movements always became worse if the animal was excited or disturbed. If one side only was cut, the abnormalities gradually subsided; if the canals of both sides were injured, the derangement of motion was permanent. These were clearly not the mere results of irritation, seeing that the symptoms continued long after the external wounds had been healed.

A great advance was made by Goltz when he suggested, in 1870, that pressure of the endolymph gives rise to sensory impressions, and that, according to the position of the body, the pressure varies by gravitation in different portions of the series of canals. He showed that the sensory impressions bear an important relation to equilibriation, and that by altering these impressions he could produce results similar to those which follow section of the canals. He fixed the heads of pigeons in peculiar positions, tying, for example, the head

down upon the breast, and found that equilibriation was thereby impaired.

The next advance was made by Cyon in 1872, who repeated and confirmed the former observations, and formulated the theory that from the semi-circular canals we derive impressions as to the position of our heads in space, each canal being definitely related to one of the dimensions of space, that these impressions guide us in equilibriation, and that failure of equilibriation may be due to disorder of their functions.

In 1875, Professor Crum-Brown published an interesting account of some experiments which he had made upon the subject. He pointed out that if the body be passively rotated, one can, with the eyes bandaged, determine pretty accurately the amount of movement made; that if such passive movements be continued beyond a certain time, the feeling is lost, but that if the rotation be suddenly arrested, the sensation of rotation continues. He suggested the theory that the sensations are due to alterations of pressure in the endolymph, not from mere gravitation, as had been supposed, but from the formation of currents in the endolymph, that fluid being conceived to lag behind in the rotational movement of the head. He pointed out how well such a theory suffices to explain the facts discovered by himself, as well as those previously known. Moreover, he remarked, that as each canal has but one ampulla, and as the same organ of sense can produce sensations differing in quantity only, and not in quality, it is probable that one canal will respond only to the rotation round one axis, and in one direction, because the sensation of rotation in the opposite direction is qualitatively different. Hence he concluded that the semi-circular canals are paired organs, and that each canal corresponds only to rotation in a single direction. The same theory was promulgated independently, and at about the same time, by Professors Mach of Prague, and Breuer of Vienna.

Some later experiments of Cyon throw doubt upon this kinetic theory, but cannot be held, in my opinion, to have disproved it.

You perceive, then, that we have abundant proof that the semi-circular canals are sensory organs subserving equilibriation, and that we are gradually acquiring definite ideas as to how their functions are performed. Besides these peripheral

structures which guide us in our equilibriation, there are, of course, conducting fibres and nerve centres which subserve the functions. Changes in any part of these structures may suffice to produce the sensory and the motor abnormality. We shall first consider the peripheral causes of giddiness, and then those due to changes in the conducting fibres and nerve centres.

In normal equilibriation we guide ourselves by information derived from all the peripheral sources to which I have referred—and in normal conditions they all harmonise—the information derived from sight, from touch, from the muscular sense, from the labyrinth, all correspond. When they do not, giddiness results. Observe, then, that peripheral giddiness is usually due to *contradictoriness of sensory impressions.*

Sometimes the contradictoriness is due to external conditions. This is especially true regarding sight. If you visit the famous Leaning Tower of Pisa, you will most likely experience, as you ascend and descend its stair, a peculiar, uneasy feeling of slight giddiness. On experiencing this sensation, it occurred to me that it was probably due to contradictoriness of impressions derived from sight and from the other sources of impression guiding equilibriation; and I found that it was so, for, by slightly altering my attitude, the feeling at once disappeared. In the tower there were three others along with me, all of whom felt the same uneasiness, and all were freed from it by altering their posture very slightly. I am satisfied from what I saw when there, and from what I have heard since, that that peculiar giddiness is felt by very many people. Some of you may have visited, and many of you will hereafter visit, the famous tower. When you do so, you will be able to verify what I have told you.

But you have all had opportunity of observing another variety of the feeling—what we may term cliff or tower giddiness. A large proportion of people suffer more or less from an uneasy feeling of giddiness whenever they stand upon a tower or a cliff, or even a steep stair or a hillside. It is due, I take it, to contradictoriness of impressions. They have been accustomed, under ordinary conditions, to receive simultaneously impressions from the plantar surfaces, from the muscular, articular, visceral, and labyrinthine structures, with visual impressions of solid ground before them; but when standing

on a tower or cliff they find the visual impressions contradicting the others, and so the peculiar feeling arises. The liability to this kind of giddiness varies in different individuals, and is determined by the sensitiveness of the nervous system, on the one hand, and by the degree in which the individual has been accustomed to trust to visual impressions for equilibriation, on the other. You will find the feeling aggravated if you look downwards to where, according to experience, the solid ground should be, and absent or diminished if you look in other directions. Some people are so sensitive in this respect that they cannot with comfort sit in a gallery of a church or theatre; some of you may feel that you cannot with comfort occupy the front gallery seat in the new Practice of Physic lecture-room in the University.

A very curious condition, manifestly allied to this, was described a few years ago by two eminent authorities, and is coming to be known to the profession as "Agoraphobia." Benedikt described it in 1870; Westphal in 1872. Its essential feature is, that while the subjects of it can walk quite well in a narrow lane, or even in an ordinary street, they become uneasy, and experience either giddiness or a peculiar feeling allied to it, when they attempt to traverse a wide market-place or square, such as narrow lanes often open into in continental towns.

Let me describe by way of illustration one of Westphal's cases. The patient was a commercial traveller, aged thirty-two, of middle height, slender, healthy-looking and mobile, and complained that he suffered greatly when he tried to walk across open squares; when he attempted to do so, a peculiar uneasiness, situated mostly in the head, but attended by violent action of the heart, was induced. On attempting to cross a square he felt as if it were miles wide, and often he trembled all over; the more he approached to the houses at the side the less was his uneasiness; a stick was no help to him, but walking arm in arm in lively conversation helped him considerably. If absorbed in thought, he could sometimes accomplish the feat; if he kept close to a carriage crossing the square he could manage pretty well; he had to deny himself the pleasures of the Thiergarten, and could not by any effort make his way to Charlottenburg (a public garden and favorite promenade in the neighborhood of Berlin). The same uneasiness

was felt in some measure if he had to walk beside a blank wall or when the shops were shut; he usually supped in an eating-house, and had to help himself home by ingenious devices; he waited till he saw people going in his direction, and followed them up, or he followed closely behind a conveyance. When asked what he would do if left without any of these external guides, he said that the very thought appalled him, but that he would probably throw himself on the ground and hold on by the grass. In his frequent journeys he had constantly to avail himself of stratagems of war, so as to be prepared under any circumstances to get assistance. On entering theatres and churches a similar uneasiness occurred at one time; but that difficulty disappeared. He could sail without much discomfort in a large vessel; not in a small boat; and could only walk at the sea-side in places where the houses come close to the shore. He lived in constant dread of these uneasy feelings. He described them as differing from giddiness and from the feeling experienced when looking from a tower. He benefited by moderate use of alcoholic stimulants. The disease began in his twenty-seventh year. The nervous system was not otherwise abnormal; but there was a slight want of symmetry of the two halves of the body. There was no marked history of nervous disease in his family.

In this patient it will be observed that there was abundant evidence of the peculiarity of the nervous organization, but the point to which I wish to draw your attention is the inability to walk across an open square, and the peculiar sensation experienced by the patient. Benedikt speaks of the sensation as giddiness, and although Westphal has drawn a distinction, as this patient did, between ordinary giddiness and this special uneasiness, I think we are warranted in believing that the feelings are closely allied.

Various explanations of the condition have been attempted, but none of them seems to be quite satisfactory. A reasonable explanation of one element of the trouble lies, I think, in the supposition that these patients, with the nervous system morbidly sensitive, have from some peculiarity acquired the habit of guiding themselves in their equilibriations by reference to near vertical lines; and that, when these vertical lines are wanting, they feel as others do when standing on the edge of a cliff. Notice the fact about the methods they devise for

getting across squares. If they can get behind some vehicle, they can walk well enough; the vertical line of the vehicle suffices to guide them.

I have met with one case of another condition allied to these. I know a lady who experiences great discomfort if she sits in a building with a lofty ceiling. She always requires to sit under a gallery in church; and the explanation is, that to her it is essential that she should have the impression of a plane not far off above her head. In these forms of giddiness you observe that, on the one hand, we have certain nervous susceptibilities more or less pronounced, combining with certain external conditions to induce this sensation. I shall now refer to some causes of giddiness with which you are probably all more or less familiar, as they occur in a large proportion of people when placed under certain conditions.

There is, first, the giddiness resulting from rapid rotation, —the waltz giddiness. This appears to be due, not so much to the contradictoriness of impressions, as to powerful impressions made upon the special centre for equilibriation, the rotation producing changes in the semi-circular canals, well explained, as we have seen, by the kinetic theory of their function. Every one naturally becomes giddy with rapid rotation, and with this, under ordinary conditions, equilibriation fails. But one may be trained to equilibriate, notwithstanding the labyrinthine impression. All physical education consists in learning to co-ordinate muscular movements. In learning to waltz, the child has not only to learn to co-ordinate certain groups of muscles, but has to learn to do so while he is receiving misleading impressions from sensory organs on which he is accustomed to rely. He has to guide his movements by the plantar, muscular, articular, and other impressions, and to time them by the music, disregarding his labyrinthine impressions altogether.

Swing-giddiness is not unfrequently experienced by children when they are enjoying that exhilarating amusement. The giddiness you will find, if you analyse it, is due to a variety of causes. There is obviously the constant changing of the visual impressions. But this is not all. The feeling is most marked when the swinger is descending. Now, during the descent, a very peculiar visceral sensation is experienced. It appears as if the body, as a whole, descended at a greater rate than the

abdominal viscera, and as if they followed; and as they followed, a certain friction took place between the peritoneal surfaces—the visceral sensation being attended by a quite peculiar uneasiness. It is probable that, in the cranium and in the semi-circular canals a similar action may take place; but these we cannot so readily determine as the visual and the visceral impressions.

In sea-sickness, with its attendant giddiness, we find many elements contributing to the result. There are visual impressions—some very susceptible persons becoming affected even when they look at the sea; but every one who suffers from it feels his discomfort increased if he watches the varying elevations of the bulwarks of the vessel and the surrounding waves, and feels the better of looking another way, or of closing his eyes. But in this condition also the visceral impressions are most important. As the vessel sinks into the trough of the wave the body seems to descend as in the swing, the viscera appearing to sink downwards at a slower rate than the body generally. And here, as on the swing, this is attended by a terrible uneasiness. I suppose that one of the great advantages of the sea-sick invalid laying himself down at full length is that he thereby diminishes the visceral movement. With the labyrinthine impressions also the nerve centres must be sorely puzzled, for from moment to moment the impression varies as the vessel rises or sinks, or rolls from side to side. The muscular sense, also, is brought into most unusual conditions, as is also the articular sense. But one other source of sensory impressions is also at fault, for the plantar pressure varies from moment to moment. At one moment, as the vessel sinks into the wave hollow, it seems as if the vessel were falling from beneath the feet, and there is almost no plantar impression; and then, again, as the vessel rises, the pressure becomes greater. In such conditions it is clear that the sensorium receives a great variety of ever-varying and contradictory impressions.

But giddiness may be due to abnormalities of the sensory structures themselves. Notice, first, some ocular causes. In illustration of this I shall recount to you a typical case seen by some of your predecessors. When I first took charge of the clinical wards as professor, I found a patient who was unable to walk or even to stand on account of fits of giddiness,

with which he was frequently seized. On examining him I found no evidence of central nervous disease, but observed that when he took his giddy turns there was always a rapid oscillating movement of his eyes. It occurred to me that this oscillation or nystagmus might cause the giddiness, and I held his eyes fixed by slight pressure. This cured the giddiness in a moment, and while it was kept up the giddiness never recurred. On further inquiry I found that the patient was a miner, and that his case was a typical one of what has been described as miner's nystagmus. The patient continued under observation for some time, but no good was done except by the mechanical treatment.

The giddiness in that case was manifestly not due to any central disease, but was simply a result of the contradictory impressions resulting from the movement of the eyes. The disease is now pretty well known. It is due to spasm from long-continued muscular strain—is indeed a form of trade spasm. The miner while at work lies on his side, and opens up the coal-seam above and beyond his head. He works also in a dim light. He has, therefore, to strain his eyes greatly, and to keep them in an unnatural position, and this nystagmus, with its attendant giddiness, occasionally follows.

You may ask me whether nystagmus always induces giddiness. Certainly it does not. It sometimes is merely associated with giddiness, the two depending upon a common cause, as in cerebellar disease. Sometimes, again, it results from cerebral disease, sometimes from disease of the retina, sometimes from disease of the cornea, occurring in childhood. In such cases, giddiness does not result, because the sight is so much impaired that the patient learns not to be dependent on the visual impressions for guidance. This is especially the case when the cause comes into operation in early life.

Paralysis of the external rectus, when of recent origin, frequently leads to giddiness from double vision; and even if the one eye be closed, a sensation of vertigo is experienced, because the muscular sense contradicts other impressions. You will often see this fact illustrated in the eye wards, but I may mention an example of it which occurred in the case of a patient whose illness I shall describe to you later on in connection with intra-cranial lesions. The patient, a young man of nineteen, naturally of robust constitution and a rather

eminent university athlete, had sustained an injury to the head, and soon afterwards observed that he saw double, and had a constant feeling of giddiness. He soon discovered that if he closed one eye, his giddiness disappeared. It was manifest, then, that the giddiness resulted from the contradictory ocular impression due to squint, which again in its turn was due to paralysis of one of the ocular nerves. The test which I should advise you to apply in such a case is the simple one of getting the patient to close one eye; if this cures the giddiness you may be quite sure that it is of the nature we are now considering. Paralysis of other muscles of the eye may, of course, lead to the same results.

I must defer till next lecture an account of the most important of all the peripheral forms of giddiness, that due to alterations in the semi-circular canals—Menière's Disease.

LECTURE II.

Gentlemen: Our last clinical lecture was devoted to the subject of giddiness, and after describing to you the nature of the sensation, I discussed certain of its causes, viz., those due to altered conditions outside the body, and those which result from abnormal peripheral impressions. At the end of the hour I was about to explain the relationship of giddiness to diseases of the semi-circular canals.

Of all the forms of giddiness from peripheral causes, the most interesting and important is that group due to causes situated in the semi-circular canals, which are commonly known as Menière's Disease, or Labyrinthine Vertigo. Dr. Menière is superintendent of the Institution for Deaf and Dumb in Paris, and by the light of the discoveries of Flourens in regard to the semi-circular canals, he concluded that many attacks which had been considered cerebral, were in reality due to disease of these organs. In 1861, he brought his observations before the Academy of Medicine in Paris. As a type of this condition, I shall cite to you one of his most striking cases. A young woman travelled on a winter night on the outside of a stage-coach, and was exposed to great cold. She was at the time menstruating. She suddenly became completely deaf. When received into the hospital wards, the principal symptoms were constant vertigo and vomiting induced by the slightest effort to move. She died on the fifth day. At the autopsy it was found that the brain, cerebellum, and cord were free from morbid change. As the patient had all at once become deaf, although she had her hearing perfect up to the time of the attack, Menière removed the temporal bones, so that he might be able to ascertain the cause of the deafness. The semi-circular canals were the only part of the labyrinth that presented any change; they contained a reddish-colored plastic lymph instead of the fluid of Cotunnius. From such observations Dr. Menière drew his first description of the disease.

That it is not always fatal the first case which came under my care may serve to show. An apprentice boy was brought into my wards suffering from most of the symptoms of Menière's disease, such as vertigo, faintness, vomiting, and reeling gait, and roaring or humming noises in the ears, with deafness of one side. On inquiry, I found that the illness had come on suddenly and been caused by a violent blow on the side of the head which the boy had received when at work. In a few days improvement set in, and in a short time the patient was well. I supposed that, in consequence of the blow, some slight hæmorrhage had taken place into the semi-circular canals, and that the blood so effused was speedily absorbed. Whether this view of the case be correct or not, you will remember that a very speedy subsidence of the symptoms may occur. In some cases, while life is not endangered, the patient continues to suffer for long periods—even for many years—and life is made almost intolerable by the discomfort it occasions.

Some recent writers on the subject, such as Dr. M'Bride, recognize several varieties of Menière's disease. And among these I mention, first, the forms due to *changes in the external ear*. Some people experience all the symptoms of Menière's disease if they have their ears syringed, and often accumulations of wax, or of eczematous secretions, produce the same result, if they be so situated as to press with force on the drumhead.

I show you to-day a patient who has several times consulted me of late. She is fifty-six years of age, and has come complaining of giddiness, pain in the head, with dullness of hearing, a feeling of oppression within the cranium, and a singing or buzzing sound in the ears. Her hereditary and social history are unimportant; but she has lately passed through very severe trials, to which she ascribes her illness. She has two sets of abnormal sensations, one constant, the other occasional or paroxysmal. The constant feeling consists in noise in the ears, uneasiness in the head, deafness, and general discomfort. The paroxysmal consists in severe fits of giddiness, with palpitation, faintness, and coldness. The giddiness is peculiar, in respect that she feels an inclination to fall backwards; and a friend who accompanied her to the infirmary says that this is not a mere sensation, but that she actually tends to fall back. If she is able to sit down and press the back of her head

against anything, the giddiness is at once relieved. Her ears were carefully examined by Dr. Graham Brown, who found that the Eustachian tubes were not readily permeable, while there was a large mass of wax in the right meatus. On this being removed, the buzzing at once ceased; and during the week that has elapsed now since this treatment was adopted, she has felt almost well, and has certainly had none of her paroxysmal attacks. Here, then, is an example of a group of formidable symptoms depending mainly upon a cause situated in the external meatus.

The second group is that *due to diseases of the middle ear,* which is generally considered to be the commonest cause of the symptoms. As an illustration, I shall cite the case of a patient who was under my care in the Infirmary some years ago, and in which I had the benefit of Dr. M'Bride's advice and assistance. The following account is in the words of that gentleman:—

"W. H., æt. fifty-eight, complained of giddiness and staggering. He is a blacksmith by trade, and exposed to sudden changes of temperature; and to this he attributes, in a great measure, his illness. For five years his hearing has been getting gradually worse. Before the patient applied for advice, he had two very severe paroxysms of vertigo, with an interval of two days between them. What occurred on these two occasions seems to have been that the patient felt intensely giddy, heard noises in his head, and lost consciousness. This happened for the first time on a public thoroughfare, and when he recovered his senses he found himself seated and being attended to by bystanders. He then felt sick, and everything round him seemed to turn (direction not observed). He staggered home, and when he got there vomited and fell asleep. On awaking he felt better, and next day went to work, feeling well. On the day following, however, he had a repetition of the attack. Since then the patient has been troubled with constant giddiness and staggering towards the left. A mixture of iodide and bromide of potassium seemed to have little or no effect on the symptoms. Except for the giddiness and staggering, the patient seemed in good health.

"The examination of the ears gave the following results:—Watch (normally heard at thirty inches) not heard in contact with either auricle. Conversation is, however, fairly well

heard, and the tuning-fork is well heard in both ears by bone conduction. Tympanic Membranes.—Right membrane opaque, with vascular injection along the handle of the malleus. Anteriorly and superiorly there is a dark atrophic patch. Left membrane indrawn, with well-marked folds. Politzer's method only succeeded in forcing air into the left tympanum. After this, inspection showed the corresponding membrane flattened out, the folds having disappeared. Air could only be driven into the right middle ear through the Eustachian catheter, and auscultation during the process revealed a distant gurgle, indicating probably an accumulation of mucus in the pharyngeal orifice of the right Eustachian tube.

"On the first attempt to inflate the tympana by Politzer's method, a very extraordinary effect was produced. As stated, air only entered the left middle ear; but whereas, before the operation, the patient had great difficulty in standing and walking, even with assistance, after the inflation he declared himself greatly relieved, and was able to walk about alone and unsupported. The subsequent treatment consisted in astringent applications to the throat and nasopharynx, which were in a catarrhal state, inflation of iodised steam into the tympana, and occasional use of the air-bag and Eustachian catheter. The result of this treatment was that in a week or two the only symptom of vertigo left was that looking down suddenly produced slight giddiness. The hearing also improved considerably; that is, he could hear a watch, which was previously altogether inaudible, on the right side in contact with the auricle, and on the left just off the ear. The tinnitus also, from which he suffered, was much relieved."

Commenting upon these facts, Dr. M'Bride says: "Now, this case is perfectly typical of what is often known as Menière's disease in an aggravated form. The vertigo, tinnitus, vomiting, and loss of consciousness were all well marked The deafness, however, was most distinctly traceable to chronic middle-ear catarrh, pure and simple. There was no organic mischief in the cochlea, as shown by the tuning-fork test, nor in the semi-circular canals, as proved by the success of local treatment directed to the middle ear. Moreover, we could trace the nervous phenomena to deficient ventilation of the left tympanum; for whenever air entered it there was an immediate and marked improvement. It was on that side, too,

that there was most evidence of altered intra-tympanal tension in the appearance of the drumhead; and we have before seen that changes of tension in the tympanum produce a more or less corresponding alteration in the endolymph. The case is important as one showing the most marked and aggravated characteristics of Menière's disease, depending upon a curable condition of the middle ear—curable, be it observed, not by empirical inunction of iodine and application of blisters, but by rational treatment directed to recognized pathological condition. I have seen a considerable number of cases where staggering and giddiness depend upon middle ear lesions of various kinds, but none so severe as in this case."

In Menière's first case the symptoms were *due to lesions of the internal ear*. The disorder may supervene in various ways quite suddenly, as in the case of Menière, or in that of the apprentice boy, already cited; or very gradually occurring in connection with chronic disease. The condition may also be fatal, or it may pass away quickly, or it may last for a long time without endangering life.

With regard to the treatment of Menière's disease, you must seek to determine the particular form of the malady with which you have to deal. If the cause be situated in the external meatus, try to remove it. If it be due to obstruction of the Eustachian tubes, seek to have them opened up. If it be due to changes in the labyrinth itself, much less can be done; but by means of counter-irritants and absorbents good results may be obtained. Charcot has spoken strongly of the advantage following the use of quinine in this disease, and remarks that it often seems to relieve the patient from the humming or ringing sounds which are so often complained of.

Lesions of the spinal cord are not very often attended by giddiness, but in cases of locomotor ataxia it is sometimes much complained of, and I have found it more prevalent in earlier stages of that disease than in the later. It may arise in various ways. Let me describe to you some cases. A very intelligent schoolmaster, resident in a country district in Cumberland, consulted me on account of spinal symptoms. I found that he had for several years had slight symptoms of locomotor ataxia; but that in consequence of overwork preparatory to inspection of his school, a degree of actual paralysis had supervened. This paralysis happily passed off in a few

weeks under treatment, but the ataxic symptoms persisted. He told me that he very frequently suffered from vertigo, but, on inquiry, it proved to have been present only when he also had double vision or actual squinting. I show you to-day also a patient suffering from locomotor ataxia. You observe that the gait is distinctly characteristic, and that, when his eyes are closed, he tends to fall. He complains much of giddiness, but this giddiness is cured when he closes one eye. It is a result of the double vision. In these cases then the cause is manifestly ocular, and referable to one of the groups already discussed. But that is not the only cause of giddiness in locomotor ataxia. It seems to result sometimes from changes in the sensory impressions, from other sources, and sometimes perhaps from changes in the brain.

Patients suffering from multiple sclerosis of the brain and cord often complain of giddiness. It may possibly result from the nystagmus, but certainly cannot be referred in all cases to this cause, for it may occur without nystagmus, and be awanting when nystagmus is present. It is apt to occur in short isolated attacks, and apart from any circumstance which seems obviously fitted to explain it.

Giddiness arises from a great variety of intra-cranial conditions, conditions varying both in respect of seat and of lesion. It occurs from lesions of the cerebellum, the crura cerebelli, the pons, the cerebral peduncles, the corpora quadrageminia, and other parts of the cerebrum, and it arises from anemia, congestion, hæmorrhages, softenings, and new formations. At the same time it must be admitted that cases may be found on record of lesion in any one of the above-named intra-cranial structures in which no giddiness occurred, and it is equally true that each of the lesions may be unattended by the symptom.

Sometimes the giddiness appears to be a direct symptom; sometimes it merely results from paralysis, especially paralysis of some of the ocular muscles, attended by double vision. It is certainly most constantly associated with cerebellar disease. The peculiar swaying or staggering gait, like that of slight intoxication, has long been recognized as a feature of cerebellar maladies, and although the staggering is not always, it is very often accompanied by a feeling of giddiness. It is said to be generally increased when the patient opens his eyes, and

relieved when he lays hold of anything. It may be present only occasionally, or when the patient is in the upright posture, but sometimes it is present even while he is lying down. As a good typical case of cerebellar disease, I select one which is recorded by Professor Nothnagel as having been observed by himself. W. P., a servant girl, thirty-six years of age, had complained since the beginning of August, 1876, of a frequently recurring feeling of giddiness. It used to come on suddenly, especially when she was walking, or when she rose from her chair, and usually disappeared in a few seconds or minutes. At the same time she used to sway to both sides, but never fell to the ground. From the beginning of September, she had severe pain in the back of the head; from the middle of September she had frequently malaise and vomiting. Later on, she had frequently humming in both ears, and she observed an unpleasant saline taste in mouth and increased thirst. In the beginning of October, Nothnagel examined her, and found that intelligence was normal, that there was almost constant occipital pain, that she always lay on her back, because when she sat up she had giddiness and vomiting. The movements of arms and hands were free and strong. The finer movements were easily performed, even when the eyes were closed. There was no abnormality of the muscles of the face, or the tongue. All movements of the limbs were rapid and precise, even with the eyes closed, and the patient knew the position of her limbs, and could point to them. She could walk if she got the slightest hold of anything; but if she were left alone, marked swaying occurred (in no particular direction), with giddiness, choking, vomiting, and the patient tumbled down if not held up. It made no difference whether the eyes were closed or open; without help she could not walk, and even with support she walked unsteadily. When giddy, the patient felt as if objects moved round her. The special senses were normal; the ophthalmoscope showed in the right eye slight venous congestion; in the left, a normal fundus. During October and November her condition remained unchanged; from the end of December she frequently had epileptiform convulsions and double vision. She died 18th January, 1877, within six months of the commencement of the illness. On the post-mortem examination, the cerebrum was found to be normal. The cerebellum was found to contain several tumors, involving

both sides and also the central part. The crura cerebelli and the corpora quadragemina were unaffected. In this case, you observe that giddiness was very pronounced, and that it preceded the occurrence of the other symptoms, was not due to squinting, and most likely resulted from the cerebellar disease.

As an instance of cerebellar apoplexy, I shall mention one observed by Dr. Brodribb of Hastings, and briefly recorded in Dr. Wilks' work on the "Diseases of the Nervous System." A lady, aged fifty-three, had travelled from London to visit a sick relative, and being depressed in spirits, had recourse, more than once, to her brandy bottle. After her arrival at the house, she went out for a drive, and on her return she could scarcely walk or stand. She expressed a fear that she was intoxicated, having partaken too largely of brandy, and her friends were at first willing to coincide in this opinion. After a few hours, however, she fell into a state of coma, and died. The post-mortem examination showed a clot of blood of the size of a pigeon's egg in the right lobe of the cerebellum. Dr. Brodribb, on further inquiry, could not learn that there had been any special loss of motion, or any disturbance of the senses, but merely a want of regulating movement, such as is seen in an intoxicated person.

With regard to the cerebellar reeling, you must observe that it is not always associated with giddiness. I lately had the opportunity of studying closely a case which I believe to be certainly cerebellar. A student, nineteen years of age, and who had been remarkably strong, and, as I was told, a leading athlete in his university, sustained an injury to his head about four years ago. At first this injury was followed by no symptoms, but soon there occurred squinting, with double vision and giddiness. This giddiness, he found, as I have already told you, that he could cure by closing one eye, and it disappeared permanently as the squint passed away, in the course of three or four months. From this time he remained free from any unhealthy symptoms, able to pursue his studies and his athletics until about six months before he came under my notice. He then observed that in walking he occasionally reeled to one side; and people remarked upon the peculiar gait, ascribing it to intoxication. But, while he thus staggered, he felt no giddiness. He noticed that the staggering was more toward the right side, and that his head tended to go in that

direction, and forwards; and he felt just as if he were making the extraordinary movement in order to maintain his equilibrium. He became unable to ride because of the tendency of his head to fall forward, a tendency which he could better overcome when on foot than when on horseback. Four months before I saw him, although other people constantly remarked upon his peculiar gait, he was able to go about pretty well; indeed, he walked a distance of six miles in deep snow, and appeared to be little the worse of it, so that his muscular vigor was evidently then little impaired. But for a marked tendency to constipation, I found all his organs and functions healthy, except the nervous system. He complained of a feeling of numbness in the limbs after exertion, but sensibility was unimpaired; his sight was good, and the fundus of the eyes normal. But he said that after walking or other fatigue his sight became indistinct. Hearing, taste, and smell were natural. With regard to his muscular sense it was difficult to speak; there was no definite proof of it being impaired, unless it be a proof that he staggered more when his eyes were closed. His skin reflexes were natural, the patellar tendon reflex slightly exaggerated; the organic, not interfered with. His voluntary movements were imperfect in consequence of a tendency to lurch to the right side and his head to pitch forward. He grasped firmly with the hand, but performed finer movements very imperfectly; in particular, could not write well, especially when tired, or when he had been attempting to study. I think that it can scarcely be doubted that in this patient cerebellar disease has occurred, probably as a consequence of the injury sustained four years ago. The gait is quite characteristic, and differs markedly from that of locomotor ataxia. I satisfied myself that he felt no giddiness even when the staggering was pronounced.

Two very interesting cases are recorded by Dr. Fraser, of Paisley, in both of which apparently an arrest of development of the cerebellum had taken place. In one, which proved fatal, the brain and cord were carefully examined, and it was found that the cortical grey substance of the cerebellum was little more than half its normal thickness, and that there were gaps at the surface, probably caused by collections of fluid in the membranes; that the white substance was less reduced in bulk, indeed appeared excessive in proportion to the grey; and that the cells of Purkinjé in the cortex were greatly shrunken and

contracted, their processes being indefinite and altered in direction.

The patient had been a healthy child till his second or third year, after which the disease had gradually developed. The first symptom was an occasional slight reel or stagger in his gait. About the age of six or seven this reeling became more marked, and almost constant. He was first seen by Dr. Fraser when about twenty years of age. At that time he was employed delivering newspapers. He walked with the gait of a very drunken man, reeling greatly, his body inclined forward, his head thrown back, apparently in constant danger of falling on his face. He was obliged to give up his occupation when about twenty-seven years of age, and was afterwards often seen running forward, then catching hold of a lamp-post, and then again going on. Although he constantly swayed about, there is no mention of giddiness in this case.

In the sister of this patient similar symptoms existed. She was unable to write in consequence of the want of power to make the necessary movements. She could not walk for fear of falling forward. Her disease had slowly advanced as the brother's did. She also was not usually affected with giddiness, indeed it was seldom a prominent symptom, except when she lay down. She then became giddy, or her sight grew indistinct. If she turned her head the feeling became exaggerated, and often she had visceral sensations, such as a feeling of nausea, but she did not vomit. It is certainly reasonable to conclude that in the female patient the lesion was the same as existed in the brother's case.

Here, then, under certain conditions, severe vertigo occurred, while usually it was not present, and apparently it was not the cause of her reeling.

Ferrier states that division of the cerebellum down the middle line, and lesions which are symmetrical on both sides, do not cause more than slight disturbance of equilibriation. Professor Schiff once showed me in Geneva two dogs on which he had performed cerebellar section. In the one, the gait was very staggering; in the other, the staggering was slight; and he told me that in the former he had injured one lateral lobe, in the latter the two lobes equally.

Ferrier has shown that where the anterior part of the middle lobe is injured, the animal tends to fall forward on his face. When the posterior part of the median lobe is injured, the

head is drawn backwards, and there is a constant tendency to fall in that direction. Ferrier satisfied himself on these points by experiments on a monkey, and clinical observations have confirmed his experimental results.

In lesions of the crura cerebelli giddiness often occurs, and the patient shows a tendency to fall towards one particular side. In illustration of this, I may cite a case recorded by Friedberg about twenty years ago, and quoted by Nothnagel in his admirable work on the Localisation of Brain Disease. A patient of six-and-twenty was, on 5th October, 1855, struck on the forehead, fell backwards upon the pavement, but was able to walk home. Fracture, with depression of the right parietal bone was found. On 15th October, symptoms of meningitis set in; the skull was trephined four weeks afterwards; the patient began to go out, and was quite well and able to work until August, 1856. Then he began to have occasional headaches, and they gradually became more severe. In October, attacks of giddiness, often attended by vomiting, came on. On the morning of the 24th of that month when he got up and was attempting to walk to the washhand-stand, violent giddiness occurred, and he was turned irresistibly to the left side, so that he could only make his way to the stand moving tumultuously, and in a half circle concave to the right. Next night he was again seized with intolerable giddiness, and suddenly began to turn round in bed on his long axis, from left to right. This was repeated five times. In the course of the same day three similar attacks occurred; first the head was turned to the right, then the thorax, then the under part of the body. When the body had reached the right side, the rotation went steadily on, the extremities sometimes followed voluntarily, sometimes seemed to strive against the movement. The eyes wandered anxiously here and there, seeking help. A complete attack lasted only a couple of minutes, as it then subsided. The patient continued to have frequent attacks of giddiness, and the feeling as if he were about to fall to the right, and as if it were necessary to support himself. On 21st November, he took a feverish turn, and his right leg and arm became paralysed. On 30th November he died. The autopsy showed the cerebrum natural, the left half of the tentorium cerebelli prominent. Under the left lobe of the cerebellum there was a rather fresh blood clot of about fifteen grammes. There was fracture of the right part of the occipi-

tal bone. There was exudative meningitis round the left lobe of the cerebellum, with red softening of its cortical substance; the inflammation of the pia mater extended along the left cerebellar peduncle to the pons, close down to that structure. The tissue of the peduncle was in a state of red softening, with small extravasations to a depth of from one and a-half to two lines; the other parts of the cerebellum, pons, and medulla oblongata were natural. In this case it is reasonable to assume that the giddiness resulted partly from the cerebellar, but probably also from the peduncular disease; the peculiar movements were characteristic of the lesion in the peduncles.

I shall cite another case which has been quoted by many writers, and was originally recorded by Belhomme. A lady of sixty had long suffered from giddiness and weakness of the legs, but was seized one day with an attack which lasted half-an-hour, in the course of which she was constantly constrained to turn round. A fresh attack followed upon great mental excitement. This time the tendency was to turn to the right. The attacks became more frequent, till at last they occurred four or five times in a day. The condition became gradually worse; the attacks assumed a pretty definite character: the patient suddenly lost consciousness, and drew herself together spasmodically; she turned herself with astonishing rapidity, usually to the right, but sometimes to the left. She died of bronchitis nearly ten years after the commencement of the illness. On examination, it was found that the middle cerebellar peduncles both showed a depression, the left more marked than the right, due to growth connected with the bone. On section through the pons, there appeared between the middle and posterior thirds a varicose injection of crescentic shape, the pons itself was one-third smaller than natural, the walls of the fourth ventricle softened and disorganised. In this case you observe that the symptom of giddiness had existed for more than ten years, and considering the character of the changes met with after death, it is reasonable to suppose that it was due to the pressure upon the cerebellar peduncles, although it may be maintained that they were referable to the cerebellum itself.

Giddiness is also observed in some cases of disease of the Pons Varolii, but I must defer illustrating this fact until the next lecture.

LECTURE III.

Gentlemen: At the end of last lecture I was about to speak of giddiness as a symptom in cases of disease of the Pons Varolii. But before doing so I wish to show you a typical case of cerebellar disease, which I am able to show you by the kindness of Professor Fraser.

You observe that, even as he stands, this patient sways about in an irregular manner. Now, when he attempts to walk he staggers like a person in a state of intoxication, and even when I make him sit down, you perceive that he seems inclined to fall in one direction or another, and then to catch himself by a sudden effort. He tells me that he constantly feels giddy, but I find that his giddiness is increased by his movements. If the back of his head is pressed against the wall, or if it is held firmly, so that the jerking is prevented, his giddiness almost, but not altogether, disappears. It is thus, then, in some degree, a consequence of the movements, but it is not entirely dependent upon them. It is due in part to some sensory change.

And now, to return to the Pons Varolii,—I shall cite in illustration one or two cases. Guéniot describes the case of a woman forty-seven years of age, who was suddenly seized with giddiness, with loss of power of speech, and paralysis of the left arm and leg. These conditions persisted. The tongue was paralysed, but there was no difficulty in swallowing, intelligence was good, and there was no affection of the facial muscles or those of the eye. Sensibility was retained in the paralysed parts—apparently rather increased; death followed in four days. On examination, it was found that the brain was natural, but the pons broken up by clot. On closer examination of the specimen it was found that while the right pyramidal bundle was completely destroyed, the left was scarcely affected. The point of interest for us in this case is the giddiness. It was manifestly a prominent feature, and it

was not the result of paralysis of any of the muscles of the eye. No cause was found excepting the lesion of the pons, and to it the well-marked vertigo must manifestly be ascribed.

Another case may be cited, which was observed and recorded by Professor Nothnagel. A syphilitic man of forty-six was seized with headache and giddiness, with tendency to fall to the left side, and loss of consciousness. After two or three attacks of that kind, he was admitted to hospital, a permanent condition having become established; there was no paralysis of face, eye, or tongue, and speech was normal; but there was complete motor paralysis of left arm, and parasis of left leg. Sensibility was unaffected. The reflexes could not be produced in the left arm. For two months there was no change, and in particular no tendency to muscular contracture. Death resulted from pneumonia; and on examination, it was found that a mass of softening, of the size of a hazel nut, was situated on the upper half of the right side of the pons, near the cerebral peduncle. In this case, also, you observe that giddiness was a prominent symptom, and that softening was the only change found on examination.

It being clear, then, that lesions of the pons itself are capable of producing giddiness, even when double vision is absent, it is scarcely necessary to adduce proof of it resulting in cases where squinting occurs. But such cases have also been observed.

In lesions of the cerebral peduncles giddiness is sometimes seen, but usually it results from squinting due to paralysis of some of the muscles of the eye. Such a case as that which I am about to state, suggests that other influences operate here. It is recorded by Rosenthal and quoted by Nothnagel. A woman of thirty-nine had suffered for two years from headache, giddiness, and dimness of sight, with paralysis of the right side. The giddiness was so great that the patient preferred the recumbent position. Severe giddiness set in if, even when recumbent, she turned on her left side. She had paralysis of the third left cranial nerve with paralysis of the lower branches of the facial and of the limbs; on the right, distinct anæsthesia. After death, it was found that a tumor of the size of a pea lay between the crura cerebri. The innermost part of the right cerebral peduncle was softened. In the interior of the left crus cerebri there was a cist of the size of a

pea, which destroyed the left third nerve, and another tumor of the size of a bean involved the right oculo motor.

I think you will agree with me in believing that although the squinting may have been a factor in the production of giddiness, there certainly was a further influence in operation, seeing that the symptom was so severe.

In lesions of the corpora quadrigemina giddiness sometimes occurs, at all events staggering gait has been observed in some cases. In illustration of giddiness from this lesion, I select a case recorded by my friend Dr. Duffin, of King's College, London. The patient was a steady and powerful man, and the earliest symptom—a sense of dragging at the back of the neck—occurred about four months before his death. The walk early became unsteady, and there were repeated attacks of vertigo which diminished when the eyes were closed. Headache and contraction of the muscles of the neck and spine were prominent symptoms. Sight soon became impaired, and blindness speedily followed with well-marked double optic neuritis. The intelligence became obscured only about a fortnight before death. He died comatose. The autopsy showed the corpora quadrigemina and the pineal body replaced by a glioma. The right optic thalamus had atrophied from pressure, and the right superior peduncle of the cerebellum was also involved. It is possible that the giddiness was connected with change in the peduncle, but considerng that the tumor involved primarily the corpora quadrigemina, and the pineal gland, and that the giddiness was an early symptom, it is more reasonable to refer the giddiness to the altered condition of the corpora quadrigemina themselves.

Besides these distinctly localised intra-cranial causes of giddiness, there are others which seem to act upon the cranial contents generally,—for example, cerebral tumor in any part of the brain may be found to produce occasional fits of giddiness, and alterations of the cerebral circulation induce a like result.

Congestion, whether of active or passive origin, induces giddiness, sometimes to such an extent as to prevent the patient from walking, and often sufficing to render quick turning round a matter of difficulty. In treating such a condition, one must first advert to the cause. If it be passive congestion, seek to remove the obstruction; if it be the result of

plethora, diminish the volume of the blood; if it be from overwork, or other undue excitement of the brain, or from a tendency to inflammation, use such remedies as cold to the head, ergotin, the bromides, and perhaps derivatives.

Vertigo is a common symptom in cerebral anæmia. It is apt to be induced when the patient suddenly changes his attitude, either by lying down or getting up. Sometimes it is merely what the patients describe as swimming in the head, at others it is well-defined vertigo. It is often associated with neuralgic and other forms of headache. You will meet with it very frequently in cases of chlorosis. Indeed it is sometimes one of the most troublesome symptoms of that disease. It is also occasionally met with in cases of anæmia due to loss of blood, slight and long continued, as in bleeding hæmorrhoids, or more formidable as in menorrhagia or other uterine complaints. Sometimes, also, it is seen in the later stages of aortic valvular disease, when the cerebral anæmia becomes pronounced; and sometimes in cases of unexplained anæmia whether referable to the pernicious variety or not, it also occurs. In these cases you will find that the patient suffers less (except when special peculiarities come into play) after food has been taken, or after a little alcohol, and that he is sometimes markedly relieved, for a time at least, by the use of nitrite of amyl. The treatment of the giddiness in such cases is, of course, the treatment proper to the variety of anæmia which may be causing it, and usually consists in checking any drain of blood which may exist, and improving the condition of the blood itself. Let me remark in regard to one of these causes—viz., the bleeding from hæmorrhoids,—that you will often have to deal as physicians with this complaint, and that I know of no plan of treatment more successful than that which I learned from Professor Oppoltzer, of Vienna—viz., the regular use of aloes and sulphate of iron. If you will direct your patient to take morning and evening, or three times a-day if it be necessary, a pill containing one grain of aqueous extract of aloes, one-third of a grain of sulphate of iron, and two grains of extract of taraxacum, you will find that free soft motions are produced, while the bleeding as a rule rapidly disappears. In this way your patients may often be relieved without having recourse to surgical treatment. I say nothing of the treatment of the uterine or other hæmor-

rhages; but should like to accentuate the fact that in the effort to improve the condition of the blood, when our chief remedy, iron, fails, arsenic often stands us in good stead.

Vertigo is sometimes due to mere exhaustion of the nervous system, as from overwork, sexual excesses, and such like; this occurs quite apart from anæmia, is manifestly a result of changes in the nerve centres themselves, and is to be treated by means of rest, good diet, and nervine tonics—chalybeates often proving unsuitable.

Giddiness sometimes results from and persists for long after injuries to the head. The patient is thrown from horseback or from a bicycle, and, falling on the head, is for a time stunned; on recovering, he is at first much troubled with giddiness or with headache, and he finds that for months, or for life, he is much more easily made giddy, becoming so under conditions in which previously no giddiness would have occurred. The nervous system has acquired a new mobility of this and of other kinds. You will find that patients who have suffered from sunstroke, even to a slight extent, often exhibit the same peculiarity.

A very distressing form of vertigo is that which is associated with epilepsy. One often meets with such cases in practice. Take as illustration a case regarding which I was recently consulted. A lady, aged forty, sustained an injury to the head about seven years ago. From that time she became subject to attacks, usually merely of giddiness, but occasionally of complete unconsciousness. On examination, nothing was found in the state of the ear or of the alimentary tract to account for the condition, and the only satisfactory explanation was that which referred the process to the category of epilepsy. Such a diagnosis as this can scarcely, of course, be established in the absence of more typical epileptic attacks. The treatment in such a case must consist of careful regulation of diet, the administration of bromides, and belladonna, and, in rare cases, operative interference at the seat of injury in the skull. You must also note that the epileptic may have giddiness as a warning at the onset of his attack, sometimes as an aura, sometimes merely as one of the early phenomena of the attack.

In other nervous affections, such as migraine, giddiness occurs. It is not in my experience a frequent symptom, but

is met with occasionally towards the end of the first stage, when the ocular or other sensory troubles are nearly passed, and the headache is about to commence. Sometimes it occurs later, when the headache is fairly developed, and the nausea or vomiting has come on. The diagnosis of the cause of the form of vertigo is easy to any one who is acquainted with the features of migraine. The treatment in such a case is of course that applicable to migraine generally; and that again is guided by a study of the cause, whether it be connected with gastric and hepatic derangements, with constipation, or with nervous exhaustion. The mention of each of these causes will suggest to our minds the appropriate remedies; but, in addition, you will find that, in many cases, the attacks may be warded off by the regular use of the bromides, or of guarana, or chloride of ammonium, or of an alcoholic stimulant, or hyoscyamus, or spirit of chloroform, or even a cup of tea or coffee.

Giddiness is often complained of by old people, particularly those affected with degenerative changes in the arteries, and in such cases is a cause of much alarm, being popularly and justly associated with the idea of a tendency to apoplexy. Whatever may be the precise pathology of this variety, I would have you bear in mind that one very able physician, Dr. Handfield Jones, has found the bichloride of mercury, in small doses, of very great service in such cases.

There is a form of intra-cranial giddiness which you can easily produce experimentally for yourselves,—viz., that described by the late Professor Purkinjé of Prague, as being produced when a constant current of sufficient strength is transmitted through the head from ear to ear. If you place the electrodes in the mastoid fossæ, and allow a current of medium strength, say ten or twelve cells, to pass, you will find immediately that giddiness results, external objects, appearing to rotate in the direction of the current, while you incline to turn in the opposite direction. It requires a much stronger current to bring out movements of the eyeballs, such as Hitzig has described. It may turn out that these changes are due to an influence exerted on the semi-circular canals; but this seems improbable, both from the locality in which the electrodes have to be placed, and from the occurrence of the nystagmus when stronger currents are employed.

With regard to the diagnosis in cases of giddiness from intra-cranial disease, I should advise you to satisfy yourselves first as to whether there is paralysis of any of the eye muscles or not, and not to conclude that giddiness is due to brain lesion unless other and more characteristic symptoms of intra-cranial disease be present.

The treatment of giddiness from intra-cranial causes, other than those already referred to, is not very promising at present. There are some cases in which the lesion being syphilitic, iodide of potassium, or mercury, or a combination of the two, are of great service; there are probably some in which the bichloride of mercury is useful, even when the disease is not due to syphilis; but on the whole, medicine is of little service. Now and then a surgical operation does good by removing some irritating fragment of bone, or by diminishing intra-cranial tension.

Having thus traced the various nervous causes of vertigo with which we were acquainted, I now proceed to describe a number of others which you will find come frequently into operation. Among those we shall take first dyspeptic giddiness. It is matter of common observation that, along with gastric and hepatic disturbance, headache and giddiness frequently occur. But there is in addition a formidable and alarming kind of giddiness, which has been well described by Trousseau in his clinical lectures, and by Dr. Ramskill in "Reynolds' System of Medicine." It is known by the name of stomachal vertigo, or *vertigo a stomacho læso.* The case generally presents such features as the following: The patient an hour or two after taking food is subjected to some fatigue, excitement, or emotion, and suddenly becomes very giddy. He reels, perhaps falls to the ground, becomes sick, may lose consciousness, or may simply suffer from a peculiar headache. He seems to himself to be turning over in all directions, or to have currents within his head, which are flowing, in a curved direction, from before backwards, or from behind forwards, or in an irregular manner. Surrounding objects seem also changed. The ground feels to his feet like the deck of a ship on a stormy sea, while other things seem to be constantly changing their position, swinging with jerks upwards or downwards, backwards or forwards; and while he knows that these are illusions, he yet cannot steady himself. Per-

haps vomiting takes place; perhaps there is a copious discharge of flatus from the stomach or the bowels; perhaps sudden diarrhœa. Then he becomes almost well, the giddiness passing off, and he is free from the illness for the time. Now, it may be that you find—as Dr. Ramskill found in one of his cases—that the patient has had a hearty breakfast, including sausages and Devonshire cream, or some other things equally difficult of digestion, or the diet may have been perfectly simple. One attack seems to render the patient more liable to the recurrence, and your patient may give you the history of many seizures of varying severity.

This form of vertigo may be transient, or may be persistent for a time. Some years ago I was consulted by a lady whose home was in a distant part of Scotland. She was little and stout, and came into the room with a curious dazed expression, puting her hand on a chair or a table at every opportunity for support, and still occasionally reeling a little like a person on board ship who has not acquired his sea-legs. She stated that life was made intolerable to her by various uneasy feelings, the billowy rolling of the floor being the most distressing; but that occasionally she had fits of unconsciousness, and sometimes convulsions. Her tongue was furred; her appetite was impaired; and she suffered from constipation. There was no deafness nor noises in the ears, nor any other condition characteristic of Menière's disease. Neither was there any fixed pain in the head, nor eye changes, paralysis, or convulsions, such as might have been indicated by cerebral tumor, and her illness had already lasted for years. I was satisfied from the result of treatment, as well as afterwards from the absence of important symptoms, that this case was to a large extent dyspeptic in its origin, the dyspepsia being implanted upon a very sensitive system. The fits of unconsciousness I regarded as syncopal, the convulsions as probably hysterical. When she was treated by means of stomachics and aperients, with regulation of the diet, she became greatly better, and now enjoys fairly good health.

A patient lately presented himself to me much alarmed about attacks of vertigo. He was somewhat advanced in years, of large frame, and had retired from professional work, which had, he told me, been laborious. As he suffered much from feelings of debility, he took food at short intervals and

in considerable quantity; being unfit for active bodily exertion, he tended to grow stout. Gradually he became subject to attacks of giddiness, associated with extreme anxiety, dimness of vision, and nausea, and even vomiting. The vomiting was attended by partial relief, and was followed after an hour or two by complete recovery. In this case also there was nothing characteristic of labyrinthine or cerebral disease, and I confidently anticipate, that with the establishment of better habits, as to diet and regimen, and with the regular use of stomachic and aperient remedies, he will quite recover.

In the treatment of dyspeptic vertigo, Trousseau had the utmost confidence in the use of alkalies and bitters; he used to give a dose of quassia every morning and at bedtime, and after meals a powder containing 5 grains of bicarbonate of soda and 5 grains of magnesia with 10 grains of prepared chalk; the powders were occasionally alternated with alkaline mineral waters, but a not unimportant part of the treatment was the insistence on careful dieting and regular bodily exercise.

Remember, then, that as to diagnosis, the hints that I have given you will guide you, and that in the treatment of this form of giddiness you will often effect a cure, and constantly obtain great relief for your patient by very simple means. Regulate the diet as to quality, quantity, and times of eating. Give aperients if they are required, alkalies, and bitters. Give stomachic remedies, such as rhubarb, bismuth, soda, and aromatic powder, followed by nux vomica, quinine, or calumba or chiretta, and the good effects will speedily manifest themselves. When there is much flatus in the stomach, carminatives often do good, and if the ordinary ones fail you will find that from ten to fifteen drops of turpentine may give great relief.

Now, what is the nature of this form of vertigo? Is it reflex? Is it a result of alterations of circulation within the brain? Is it a result of poisoning? It is impossible, in the present state of our knowledge, to answer these questions definitely, but I lean to the opinion that it is of the nature of poisoning, that in connection with the chemical changes of the digestive process under certain conditions, some substance is developed which, like alcohol or tobacco, acts upon the nerve centres so as to induce the peculiar uneasiness.

Among the commonest form of vertigo must be reckoned

the toxic, and among them those due to alcohol and tobacco. When the action of alcohol has reached a certain point giddiness is experienced, and associated with this is the reeling gait. Objects may appear to whirl round the patient, or he may appear to be rotating—the movement may seem to be irregular, or in certain definite directions, as from right to left, or from left to right. You know the case of a well-known legal luminary in bygone days, who was found by a friend standing rather unsteadily in the square in which he resided, making no progress towards his door. When interrogated as to his object, "Don't you see," said he, "that the square is going round and round? and whenever my door passes I'm going to jump in." Or the apparent movement may be a rotation on a horizontal axis, as in the case of the man who was found lying on the ground, and who explained that the earth was turning rapidly round, and he was holding on by the grass to prevent it. We may not be in a position at present to state positively how this giddiness is brought about, whether through alterations of the vascular system, or by direct influence upon nerve centres, but the latter seems to me the more probable explanation. The effect of tobacco on those unaccustomed to its use is similar to that of alcohol in the production of giddiness; and other toxic agents might be mentioned which induce a like result—such as stramonium, belladonna, hydrocyanic acid, lobelia, hyoscyamus, and veratrum viride.

Occupying an intermediate position between the toxic and the dyspeptic, and perhaps also related in some measure to the labyrinthine vertigo, is the variety occasionally met with in gouty patients, sometimes slight, sometimes really severe, and which is apt to occur in the intervals between regular attacks of gout, especially as the attacks draw near, and which is often absent for a considerable time after the typical seizure. This form is, in my opinion, often referable to the stomach, but it may also perhaps be induced by toxic influence upon the nerve centres.

Besides these obviously toxic forms of vertigo, there are others which are reasonably to be referred to the same category—I mean the giddiness occurring in acute specific diseases. In the commencement of fevers, the symptom is not uncommon—just as we have commonly rigors and headache, and

occasionally convulsions, as initial phenomena. It has been remarked that in influenza it is frequently very troublesome; —sometimes as one of the earliest indications of morbid action; sometimes during the height of the disease; and that occasionally it continues for long after the acute stage of the malady has passed. It bears the same relationship to many acute diseases. In some of these cases, it is probable that at first a direct toxic influence is exerted, while at a later stage exhaustion of the nerve centres may be regarded as the most likely cause. In the case of influenza, it may be reasonably assumed that catarrh of the Eustachian tubes accounts for it. In the way of treatment you will do well to keep the patient at rest and in the recumbent position, as free as may be from the exciting causes of giddiness; for you will find that sitting up or attempting to read will often suffice to induce an attack. During the later stages, tonics and nutrients, with moderate doses of alcohol, prove most serviceable.

Vertigo is sometimes produced by violent fits of coughing; sometimes by violent fits of sneezing. I do not know for certain the explanation of the fact; it may be due to changes in the ear, possibly to changes within the sensorium. It is not of very frequent occurrence. I think it is most likely due to the first-mentioned cause operating through the Eustachian tubes. The correctness of this view could be easily tested if one were to meet with a patient subject to the symptom who at the same time had obstruction of these passages.

In some cases giddiness is due to peripheral irritation, and that irritation may be situated in various parts of the body. As a typical example, I select the giddiness which sometimes results from the presence of worms within the alimentary system. You are aware that other nervous symptoms, such as convulsions and cough, arise from this cause, and we may assume that the vertigo is brought about in the same way as these other symptoms. It is most reasonable to refer them, in the present state of our knowledge, to reflex action, and in the case of giddiness, to an influence upon the cerebral circulation. The treatment in such a case is, of course, obvious. Let the irritating cause be removed from the intestine, and the giddiness will disappear.

Vertigo arises in some individuals from purely mental causes. A patient goes on board a steamer, and although there is no

tossing, and no perceptible vibration, the recollection of what he has suffered before, or the sight of the oscillation of the waves, makes his head swim, or renders him actually giddy. In some, giddiness supervenes if a child is seen whirling rapidly round. I have known it even produced by another person walking in a small circle. The very thought of giddiness suffices in some to induce the sensation.

We have thus passed in review the chief causes of this sensation. We have considered giddiness as arising:—

(*a*) From external conditions.
(*b*) From changes in the sensory structures.
(*c*) From changes in the conducting fibres.
(*d*) From changes in the central nervous system.
(*e*) From dyspepsia.
(*f*) From toxic causes.
(*g*) From causes of uncertain seat.
(*h*) From peripheral irritation.
(*i*) From mental causes.

By following out the indications which I have given, you will generally be able to determine with certainty the particular cause in any individual case, and thereby be able to devise a rational treatment.

A CRITICAL STUDY

OF THE

Clinical Value of Albuminuria in

BRIGHT'S DISEASE.

BY

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PREFACE.

During my last year of service as interne under Professor Dieulafoy, I often had occasion to study renal affections, and I was frequently surprised to find that statements which had been accepted as classical facts were in reality not such at all. We have thought it might be useful to collect our experiences in a single monograph in order to fix, after a definite fashion, the question of the connection of albuminuria with Bright's disease, including under this term, as does my teacher, all the chronic inflammations of the kidneys.

What clinical value should we to-day accord to the symptom albuminuria in Bright's disease? Such is the question we have endeavored to answer, and to which we will try to reply at the end of our critical study.

We have opened our study by a chapter devoted to chemistry, for it has seemed essential to precede our clinical study of albuminuria by a chemical study of albuminous urines. In this first portion of our work we have sketched quite completely the methods of examining the urine. In this work we have never forgotten that we should not be chemists but only clinicians occupied with chemistry.

We have next taken up the clinical study of the symptom

albuminuria in Bright's disease, and this portion we have divided into two distinct parts of unequal importance.

In the first part we have noted, at the outset, the fact that albuminuria has lost its old diagnostic value; next we have aimed to find out its actual value, taking successively into consideration its existence, nature, and its relation to the urinary secretion and to the general state of the patient.

We have finally reached the conclusion that albuminuria, while it is alone of limited value as a symptom, is, when associated with the other symptoms of Bright's disease, of decided importance.

In the second part we have endeavored to weigh the prognosis of albuminuria in case of Bright's disease. We have been obliged to admit that the presence of albumin in the urine is of slight importance, and that not it, but the toxicity, so to speak, of the urine should be the guide to our prognosis.

After relating experiments which have seemed to us of interest, we have stated in our last chapter the actual clinical value of the symptom albuminuria in Bright's disease.

VALUE OF ALBUMINURIA IN BRIGHT'S DISEASE.

CHAPTER I.

THE METHODS OF DETERMINING ALBUMIN IN THE URINE.

The examination of the urine for albumin is to-day a rigid rule of practice, but the belief is current that the search requires few precautions, and that it is devoid of difficulties. Every day clinical errors are committed which are very prejudicial; every day the physician is mistaken by not discovering the albumin which exists, or by finding it where the urine does not contain it.

This is the reason why it seems essential, before entering upon the study of Bright's disease, to dwell somewhat at length on the precautions which should be taken in the determination of albumin in the urine.

Separation of the Mucin.

When we wish to test a specimen of urine for albumin it should first be filtered, in order to separate the mucus which is present even in normal urine (in small amount, true enough) and which is always found in large enough proportion in albuminous urine.

Usually the mucus is found in the form of a slight cloudiness, which settles little by little to the bottom of the bottle and which is readily recognized when looked for by transmitted light. At times, when the quantity of mucus is very large, the cloudiness becomes very marked, and, after an interval, a mu-

cous sediment, more or less abundant, forms, and after a little practice the quantity may be approximately determined. When the urine is filtered the mucus remains on the filter paper as a viscous mass having the appearance of varnish after desiccation. Nevertheless, after filtration there always remains a certain amount of mucous matter in solution which gives the chemical reaction of mucin. This should be at once eliminated, for in certain of its characteristics it resembles albuminoid matter, which might lead to error and cause us to think that albumin is present when it is not. In order to accomplish our purpose we have at our disposal the basic acetate of lead and acetic acid.

The basic acetate of lead, in solution, poured in small amount into urine, determines an abundant whitish precipitate which may be separated by filtration. The urine may be considered as containing no more mucin when, tested again by the lead solution, it gives no further precipitate. It is then perfectly clear, free from mucin, but it contains lead, which must be eliminated by the sulphide of hydrogen, which precipitates the lead under the form of black sulphide, which is separated by filtration.

This process, recommended by many writers, has many objections: in the first place, the basic acetate of lead, although it precipitates the mucin, does the same by many salts (the urates, the phosphates, the chlorides, etc.), so much so that one to two drops of this solution causes an abundant whitish precipitate. Further, in order that the precipitation may be complete, considerable time is required. Finally when, after filtration, we wish to eliminate the lead, the obstacles are many; the elimination, in order to be complete, requires at least two days. For these reasons we have given up this procedure, scarcely practical from a clinical point of view.

The acetic acid reaction remains. Although its value in eliminating is open to discussion, since it only precipitates incompletely, we do not hesitate to give it the preference; it is besides the only procedure recommended by chemists whose competence is not in dispute, such as Wurtz[1] and Neubauer and Vogel.[2]

When to a urine containing mucin we add acetic acid, a uniform cloudiness is obtained, which becomes much more visible if, following the advice of Lobisch,[3] we add in addition

to the acid, a small amount of iodine. This cloudiness only disappears on the addition of an excess of acid, never under the influence of heat (characteristics which differentiate from precipitates of uric acid or of acid urates, forming in excessively acid urines); it disappears, on the other hand, instantaneously and completely if at once a few drops of chlorhydric acid are added.

Only exceptionally and after long standing is a flocculent precipitate seen. Nevertheless if, before the addition of acetic acid, the urine has been diluted a number of times by its volume of water, there appear (when the quantity of mucin is not too small) quite large flocculi which under the microscope appear as quite fine granular masses containing a few crystals of uric acid. By proceeding thus the cloudiness due to urates is never obtained, and to this we will refer very shortly.

Verification of the Reaction of the Urine.

The urine having been made perfectly clear, and been entirely deprived of mucin, the reaction must be tested, and this is readily accomplished by means of litmus paper. The kind we recommend is that slightly tinted, a blue bordering on red; such a paper, prepared after Berthelot's method, besides being exceedingly sensitive, has the advantage of answering in all cases; it reddens distinctly in acid urine, and turns blue besides in alkaline urine; the result is instantaneous and the test is of the simplest possible kind.

The urine should be acid; it should redden distinctly the test paper, the color should be a frank red and not a reddish violet. Now frequently enough in cases of Bright's the urine is neutral or alkaline; if we do not wish to fall into error, therefore, it is necessary after having tested to acidify if need be by the addition of acid. Two acids have been recommended for this purpose: nitric and acetic acid.

The first has the great disadvantage of precipitating albumin if added in considerable quantity, and it renders void other reactions if added in great amount. This latter point is important to recognize, else we may fall into great error; we insist on this point, since many examiners appear to ignore it.

The fact, however, has been for long proved by Professor Jaccoud: "When you add," he says, "to albuminous urine a drop of nitric acid, this urine will not precipitate on being

heated;" and the same point has been noted by Bence Jones. This artificial and exaggerated acidity of the urine causes some modification or other of the albumin, which takes away its property of coagulation on boiling; and the proof is that if we add to the boiling clear urine a little dilute ammonia, in order to bring it back to its normal acidity, the latent albumin appears as a precipitate. This fact, little known, is most interesting; it proves that nothing can take the place of the test by litmus paper.[4]

Esbach[5] has latterly clearly proved the same point. By his directions, let us place in a graduated tube 10 cubic centimetres of a urine rich in albumin (containing, for example, 15 to 20 grammes to the litre) and then add two drops of nitric acid and heat; no cloudiness occurs.

This experiment, which we have over and again performed, must be emphasized, for it brings into strong relief the fact that a very small amount of nitric acid added to an albuminous urine completely prevents the coagulation of albumin by heat. Whatever the reason, whether it be due to the dissolution of the salts in combination with the albuminoids, as Albert Robin claims,[6] or not, the fact is well established, and it suffices to cause us to reject absolutely the use of nitric acid for the purpose of acidifying the urine of Bright's disease.

Acetic acid, on the other hand, does not precipitate albumin, and in nowise prevents its coagulation by the reagents ordinarily used; and therefore it is customarily used.

Certain precautions are still necessary in the use of this acid; it should be added only drop by drop, shaking the urine constantly, and we should cease adding when the reaction is clearly acid; an excess of acid stops completely the precipitation of the albumin. Acetic acid, we know, produces in most specimens of urine a uniform cloudiness which does not disappear on the addition of an excess of acid; this cloudiness, which may readily be mistaken for an albuminous precipitate (Reissner), is due to mucin; by acting as we have advised—that is to say, by clearing the urine of this substance—error is not likely.

Determination of the Albumin.

It is only after the two preliminary experiments which I have stated that we should proceed to search for albumin.

Many methods have been proposed; I will only mention the principal ones, dwelling particularly on those which are habitually resorted to, and these are heat and nitric acid.

Heat.—Under the influence of heat albumin coagulates; a large amount results in a flocculent precipitate, and a small amount produces a more or less marked cloudiness. The clear urine is poured into a tube half full; holding the tube by the base the upper part is alone heated; at 50° to 60° a distinct cloudiness is observed, the more readily recognized since the lower portion of the urine is clearer, and later on, at 75°, the albumin coagulates. (These two distinct phenomena possibly result from the successive coagulation of the globulin and the serin.)

After this first attempt the urine is entirely heated and allowed to settle; the albumin gathers in more or less numerous flocculi at the bottom of the tube.

The cloudiness or the precipitate thus obtained has the characteristic of not disappearing on the addition to the hot urine of acetic acid drop by drop. This verification should be resorted to in every instance, for if under these conditions (heat and moderate acidity) there results or there persists a cloudiness, however slight, the urine certainly contains albumin.

This simple process may, however, give rise to errors which it is well to bear in mind. Under the influence of heat there occasionally forms in non-albuminous urine a more or less accentuated cloudiness, sometimes even a precipitate. This latter is due to the presence of phosphates (usually the bi-basic phosphate of lime) retained in solution by free carbonic acid. This gas being expelled by the heat the phosphates precipitate in flocculi which at first sight it is difficult enough to distinguish from coagulated albumin. In case the verification just spoken of is here resorted to, as soon as a few drops of acetic or of dilute nitric acid are poured in the urine becomes clear, and concomitantly, if the urine be hot, bubbles of carbonic acid are given off.

In other instances, albuminous urines give no precipitate by heat; they only become cloudy or milky; yet when to the boiled urine nitric acid is added to strong acid reaction a precipitate forms.

This happens most frequently in case of alkaline or neutral

urines; the occurrence is exceptional in acid urines. This source of error is thus readily avoided if care is taken as we have advised to test the reaction of the urine.

Nitric Acid.—When nitric acid is added to an albuminous urine a precipitate is at once formed; in case the urine contains much albumin the precipitate is white and abundant; sometimes the urine becomes solidified; in these instances there can be no doubt as to the presence of albumin.

The same does not hold true when the urine contains but little albumin; in such a case a slight cloudiness may escape notice, or a cloudiness due to urates may simulate an albuminous precipitate; the urates, indeed, becoming decomposed by nitric acid, occasionally form a greater or less cloud; but this disappears on the addition of acetic acid and there results with ammonia the reddish-purple color which is characteristic of uric acid.

When nitric acid is used for the test, it is poured in slowly in order to allow the reaction to form; in order to obtain the maximum effect it is usually sufficient to use the acid in the proportion of 1 to 10 of the urine. If much more of the acid is used the albumin is almost at once transformed into xanthoproteic acid, the orange yellow color of which may readily veil the presence of the substance for which we are searching.

Furthermore, if we have reason to suppose that albumin is present in trifling amount it will be wise to resort to Gubler's [7] or to Heller's [8] method, or, better still, as we are personally in the habit, to the following method, which is a modification of Heller's; it is, in fact, a very delicate method and requires only a small amount of urine.

In a graduated tube pour 1 to 2 c. c. of nitric acid and then let glide, drop by drop, along the side of the tube the urine which we are testing. If this experiment is carefully performed the result is very perfect; we obtain, from above downwards:

A layer of acid, perfectly clear, colorless;

A colored line at the level of the junction of the urine and the acid;

At the same junction, if albumin be present, a whitish ring more or less pronounced is formed.

Below this is the urine, clear or cloudy from deposit of urates.

Heat and Nitric Acid.—Heat and nitric acid, such are

the agents daily in use in the search for albumin. Since each alone may lead to error, it is customary, in order to obtain a positive verdict as to whether albumin be present or not, to resort to each successively. This custom dates back almost to the discovery of the symptom which forms the object of our study.

Wells,[9] in fact, one of the first to study this interesting question (1798 to 1812), having determined over and again that the same urine tested successively by heat and by nitric acid did not always behave in the same way, advised that every specimen of urine should be subjected to the two tests. This advice, which has met with the approval of his successors, is very just; and to-day, therefore, it is a matter of routine.

Now that we are amply familiar with these two methods of use clinically, the worth of which is unquestionably very great, especially when they are associated, we deem it essential to sketch briefly the other methods which have been advised for the determination of albumin in the urine. They may be all ranged under one or another of the following:

The first aim at simplifying the *modus faciendi;*

The second are useful for determining traces of albumin which would not be revealed by heat and nitric acid.

Methods for Simplifying the Test for Albumin.

Although the methods in routine use are very simple and require neither much time nor complicated instruments nor reagents, it is an established fact that although they may readily be resorted to in hospital work they are ill adapted for private practice, at least *ex abrupto;* whence loss of time and the lack of a point essential for the completion or the affirmation of the diagnosis.

Professor Potain [10] recommends the heating of the urine in an iron or a silver spoon over a spirit lamp or the flame from cotton in a saucer of alcohol; then to instil into the urine a few drops of vinegar from the end of a match.

Less summary methods have latterly been recommended by Hindenlang, Hoffmann, and Oliver.

Hindenlang [11] recommends metaphosphoric acid, which can be much more readily carried than nitric acid; it may be obtained in the shape of crayons, which may be carried in a

glass tube. Before use the end of a crayon is to be dipped for a few seconds in 2 to 3 c. c. of water, and we thus obtain a solution of metaphosphoric acid, which at once precipitates albumin. The crayon need only be dried and replaced in the tube.

We have used this method on several occasions, have always obtained very satisfactory and very rapid effects, and we therefore recommend it in the belief that it will often render signal service.

An equally satisfactory method is that recommended at about the same time by Hoffmann[12] and Oliver;[13] it is a trifle more complicated than the preceding, but we can by means of it determine rapidly if a given specimen of urine is albuminous or not.

The reagents of use are prepared as follows:

Strips of paper are plunged into a solution of citric acid, and others into a bath of potassio-mercuric prepared as follows:

1. Corrosive sublimate, . . 1 gramme
   Aquæ destil, ... 20 grammes

Solve

2. Iod. potass, . . . 1 gramme
   Aquæ destil, ... 2 grammes

Solve.

Mix the two solutions and the result should be a clear fluid.

The strips of paper are to be dried after having been impregnated with these solutions.

To test the urine: verify its acidity: if it is not frankly acid, if it does not color test paper brick-red, acidify with a citric acid paper. This point must never be neglected, else the result will be erroneous. Next place the reactive paper in the urine, and if albumin is present (even in feeble proportion, 0.50 gramme to the litre) it is precipitated to the bottom of the test tube.

Methods Intended to Determine Traces of Albumin.

As there are many such methods, we will only describe those which seem to us to be of value.

This review may, at first sight, seem useless, but I believe that on reflection its value will be apparent.

Albumin, indeed, (a point which unfortunately is too little recognized, but which to me is incontestable) is not always precipitable, even in instances where the disease in its symptomatology is characteristic. There results this highly important fact: We should not rest content with a single test, but should always make control tests by other reagents; by following such a course we will often determine albumin where otherwise it would not have been noted.

This point established (and this is our justification for the details, possibly too technical, on which we enter) let us examine the various reagents recommended for the detection of small amounts of albumin.

Acetic Acid and Sulphate of Soda.—Into the albuminous urine dilute acetic acid is poured to a strong acid reaction, and then an equal portion of a saturated solution of sulphate of soda is added; the upper part of the mixture is next heated to boiling. The albumin is coagulated.

This method, which was recommended by Méhu,[14] gives excellent results; by means of it, indeed, an appreciable cloudiness of the urine is obtained when heat and nitric acid reveal nothing. In certain cases, however, as has been clearly proved by Bretet[15] of Vichy, this method does not reveal albumin which heat and nitric acid will. The method of Méhu, however, should not therefore be rejected, for it is certainly more sensitive than the usual reagents; the *modus faciendi* need only be modified. Méhu's method should first be used; if the result is negative add to the hot urine fifteen to twenty drops of nitric acid; a slight cloudiness will then appear, which will increase as the urine cools.

This double test is absolutely indispensable in order to affirm positively the absence of albumin. We will take occasion here to lay stress on the fact, again, that it is essential to test the urine in various ways.

Acetic Acid and Ferrocyanide of Potassium.—As in the former method acetic acid is poured to a strong acid reaction, and then a few drops of ferrocyanide of potass are added; in case albumin is present it is shortly precipitated in a flocculent form.

Acetic Acid and Phenic Acid.—To the urine is added three per cent. of nitric acid and ten per cent. of the following solution of phenic acid:[16]

Acid: Phenici	} āā 1 part
Acid: Acetic (commercial) .	}
Alcohol (90°)	2 parts

Shake and let settle.

Aceto-picric Acid.—The aceto-picric reagent is prepared by strongly acidifying with acetic acid a saturated solution of picric acid in distilled water. The urine is poured into a test tube and the acid is added drop by drop until no more precipitate forms; heat to boiling for some minutes.[17]

Picric Acid.—Into a test tube containing a concentrated solution of picric acid the filtered urine is poured drop by drop.[18]

If a cloudiness at once appears and this does not dissolve on shaking the tube, then we are dealing with albumin;

If the cloudiness is slight and not instantaneous it is usually due to the precipitation of uric acid (sometimes to the precipitation of certain medicinal alkaloids). This will be prevented if, before adding the urine, we heat the reagent slightly.

Chlorhydric Acid and Chloride of Sodium.—When the suspected urine is highly colored it is well to use the following reagent, which is highly spoken of by Roberts:[19]

Acid: Chlorhydric (D. 1.052). .	1 volume
Aquæ.	16 volumes

M.

With this mixture a saturated solution of chloride of sodium is saturated and filtered; the reagent is then ready.

Pour the saline solution into a test tube and add the urine; the presence of albumin is indicated by the formation of a cloudiness at the point of contact of the two fluids, and this cloudiness disappears on the addition of water; the albumin never coagulates.

Bichloride of Mercury.—A few drops of a 100 per cent. solution of bichloride of mercury is poured into the urine (an excess will redissolve the albumin) and heat; very rapidly a precipitate is formed which increases on boiling.

Bichloride of Mercury, Iodide of Potass and Acetic Acid.—Tauret[20] has advised the following reagent, which bears his name:

Iodide of potass	2.32 grammes
Bichloride of mercury . .	1.35 "
Acid: acetic	20 c. c.
Distilled water q. s. ad . .	64 c. c.

M.

This reagent is poured into the urine. A cloudiness forms. Heat and the precipitate remains, or else a granular precipitate forms which, after awhile, collects at the bottom of the tube.

This reagent, used to a great extent in France, has many disadvantages on which Professor Jaccoud has dwelt, with justice, at his clinic at Pitié:[21] "Many things are precipitated besides albumin." Indeed the reagent precipitates alkaloids and peptones; although these disappear on heating (a characteristic which differentiates from true albumin) it is better not to use this reagent; for, as Jaccoud says, "this reagent is dangerous, for the reason alone that it is essential to control it by other tests."

Such are the chief reagents recommended for the determination of albumin. What is their respective value?

G. Oliver[22] and Tyson, in a communication to the Philadelphia Medical Society, have tried to answer this question. The following, in a few words, are their results:

	Parts of liquid.
Sol. of picric acid revealed 1 part albumin in	20,000
Acidulated sol. of chloride of sodium " "	12,000
" " ferrocyanide of potass " "	10,000
Nitric acid " "	7,000
Heat " "	6,000

Let me add that, according to Tyson, heat combined with nitric acid reveals amounts of albumin inferior to those obtained by the use of one or another of the other agents alone.

Their sensitiveness is thus very great, especially that of the solution of picric acid; unfortunately it exposes to a number of errors which it is important to recognize.

The picric acid solution may redissolve the albumin when it is abundant; it yields a precipitate in the urine of patients taking quinine; it precipitates peptones.

Therefore it should not be used alone.

We see, then, finally, once again, that we ought always,

before affirming the presence of albumin, to make comparative tests with various reagents.

Determination of the Nature of Urinary Albumin.

It is not to-day sufficient to determine albumin, it is also essential to find out the variety of albumin which is present in the urine.

This question of the determination of urinary albumin is really of recent date, although it has been studied for fully thirty years.

Mialhe[23] was the first, as far as we know, to prove the existence of three kinds of albumin, each characterized by the nature of the albuminous matter in the urine.

We may find: *a.* Normal albumin, coagulating perfectly by heat and nitric acid, and not redissolving in an excess of acid; *b.* Modified albumin (amorphous or caseiform) imperfectly coagulated by heat, and forming with nitric acid a precipitate which is redissolved in an excess of acid. "This second variety," he adds, "is formed particularly in Bright's disease"; *c.* Albuminose, coagulated neither by heat nor by nitric acid, but by tannin, by creosote, by alcohol, by salts of silver and of mercury.

Mialhe's opinions are stated in two theses presented to the Faculté de Médécine, that of Dr. Mozian[24] and that of Dr. Ducom;[25] both insist on this little recognized clinical fact, and urge that the different kinds of albumin in the urine be sought for with greater care.

Nevertheless, the question was neglected in the years which followed, even by the writers who studied in particular albuminuria. In looking over the excellent article which Gubler wrote on this subject in the *Dictionnaire des Sciences Médicale*, 1865, we find that there does not exist a single kind of albuminuria. "This agent," says Gubler (page 516 and 517), "varies according to the case, and the urine in the same individual may contain various forms united. Some coagulating by heat and nitric acid, like egg and serum-albumin, others by heat and nitric acid together, and redissolving in an excess of acid, others finally not coagulable by heat but precipitable by nitric acid. Still," he adds, "the determination of these different kinds of albumin has as yet no clinical importance,

since not one is specially attached to Bright's rather than to other true albuminuria, and since albuminoid agents are readily transformed the one into the others under the influence of purely accidental causes."

Gerhardt[26] first proved that in urines not coagulable by heat and by nitric acid, a precipitate sometimes followed the addition of absolute alcohol due to the transformation of serum-albumin into peptone; he gave to this precipitate the name of latent albuminuria.

Next the chemist Lehmann[27] showed that by passing a current of carbonic acid gas through an albuminous urine a precipitate would form, having all the characteristics of globulin. These experiments were fully confirmed by Edfelsen[28] and by Senator,[29] who endeavored to find in albuminous urines all the albuminoid elements of the blood, as also Fuhry-Suethlage,[30] who with the same end in view performed a number of interesting experiments by dialysis.

It is only of late years that this question has been envisaged in our country.

Professor Lépine, of Lyons, was the first in France to study the albuminoid elements in urine; in 1880, by his assistance, appeared two theses containing the results of the experiments made at the Lyons school, the one written by Dr. Dauvé[31] and the other by Dr. Estelle,[32] and they proved that there were two varieties of urinary albumin: serin and globulin.

At the end of the year 1880 Charcot,[33] in his lectures on pathological anatomy at the Faculté de Médécine, said that in albuminous urine might be met, aside from serum, albumin or serin, globulin, and even peptones, as had long before been claimed by Gerhardt, and as had been confirmed by the experiments of Maixner[34] and by Hofmeister.[35]

Next, Flavard[36] and Faveret[37] finished the study of globulin; Nourry[38] and Wassermann[39] considered the question of peptones, which had been so thoroughly studied in Germany by von Jacksch.[40] Recently, Professor Jaccoud[41] has insisted particularly on the importance of searching for and of specifying the different kinds of albumin in the urine and has described at considerable length the different procedures to be followed in this direction.

Shortly afterwards Dr. Bengines-Corbeau[42] of St. Michel (*sur* Aisne) published a biological chemical study giving a complete *résumé* of the question.

Finally last year there appeared about the same time in France and in Italy a review of the clinical value of the different varieties of albumin in the urine.[43]

The fact then is perfectly established to-day that there does not exist a single kind of albuminuria; but that there are albuminurias.

The Different Kinds of Urinary Albumin.

"Making every allowance for further investigation (for the subject is not as yet completely settled) we may say to-day that there are three varieties of albumin to be considered in pathological urine."[44]

This expression of Jaccoud's in 1885, which was an echo of what Charcot said in 1880, remains perfectly true; there are three principal varieties of albumin in the urine: serin, globulin, and peptones; there are others but little known as yet and on which we will not spend time, except in regard to hemialbuminose or propeptone, the history of which is about emerging from chaos.

Serin, identical with the serum of the blood, forms the most important of this group of substances. Albuminoid in nature, because it is constantly present in albuminous urines; in forty-one analyses of urine from renal affections made in 1876 by Petri[45] of the Berlin clinic, it was found forty-one times.

Serin, "the most pathological of the albumins, the Bright's albumin, *par excellence*" (Jaccoud), presents all the characteristics of albuminoid substances; it is analogous to egg-albumin; it differs, however, in the facts:

It gives no precipitate with ether; while egg-albumin precipitates in large lumps.

It redissolves completely in an excess of nitric acid; and this is not the case with egg-albumin. This latter fact it is important to remember, for it allows us, by the simple examination of the urine, to formulate the diet proper to the patient.

Globulin is far less frequently found than serin in albuminous urines (thirteen times out of forty-one; Clin., Berlin).

This albuminoid substance forms the most common type of the large family of globulins which to-day, according to chemistry, contains a large number of albumins formerly considered to be distinct species: dissolved fibrin, fibrino-plastic sub-

stance, casein of serum, hydropisin, crystalline, etc. Although its true name is paraglobulin (Kühne), it is commonly known as globulin (Weyl and Hoppe-Seyler); it has received this name because allied to hematin it constitutes principally the substance of the blood corpuscles.

Globulin presents the common characters of serin, coagulation by heat and by nitric acid; but it possesses also certain characters peculiar to itself which it is important to know:

It is more diffusible than serin; it passes through membranes with a facility equal to white of egg.

It is converted into concrete fibrin when, in contact with the air, it is mixed with a solution of fibrinogen.

At the end of three to four hours it becomes flocculent under the influence of a current of carbonic acid gas; but it redissolves when air or oxygen is introduced into the mass.

It is precipitated from cold urine when this is supersaturated with crystallized sulphate of magnesium.

The third variety of urinary albumin, described by Mialhe under the name of albuminose, of latent albuminuria by Gerhardt, and latterly by Lehmann under the name peptone, occupies by its frequency the second place in the urinary albumins, as witness the statistics cited twenty-eight times out of forty-one—that is, about two-thirds of the cases.

Of late years many monographs on peptones have appeared: in Germany, Maixner,[46] Hofmeister,[47] von Jacksch;[48] in Italy, Pietro Grocco,[49] Lussana,[50] Mya,[51] Primavera;[52] in France, Henninger,[53] Nourry,[54] Wassermann,[55] Georges,[56] Bouchard,[57] and they are differentiated from the other albuminoid substances in the urine by the following characteristics:

They do not coagulate by heat and acetic acid, nor by nitric acid, nor by the acetic solution of ferrocyanide of potassium, nor by any reagent ordinarily used in the tests for albumin.

They are coagulated by absolute alcohol as a flocculent precipitate which is redissolved by water, even though the masses have remained long in alcohol.

There remains a third urinary albumin; this is hemialbuminose or propeptone. Although far less known than the preceding, it forms a substance intermediate between ordinary albumin and peptones. As described by various writers, Salkowsky[58] and Lepine[59] for example, it has certain characteristics by which it may be recognized:

It does not coagulate by heat.

It coagulates when cold by nitric acid, by ferrocyanide of potassium and even by chloride of sodium in excess, in the presence of acetic acid.

Serin, globulin, peptones, propeptone, such are the principal varieties of albuminous substances which may be met with differently commingled in the urine of Bright's disease. Now that we have determined their distinguishing traits, it is time to expose the different ways of distinguishing and of differentiating them the one from the other, and we will be obliged to consider this at length, for their study is as yet hardly classical, and their determination often very delicate.

Means of Determining and of Differentiating the Various Kinds of Urinary Albumin.

Whenever we suspect the presence of albumin in the urine it is necessary (after having eliminated mucin, and after having verified its reaction) to test by heat and by nitric acid; under this test, according to the case:

There forms a precipitate. No precipitate forms.

In case of the first instance it is necessary to determine the nature of this precipitate, which may be due to serin, or to globulin, or to both simultaneously.

In the second instance it is necessary to prove by different tests that there is really no precipitate, that is, to search for peptones.

(Since hemialbuminose is rarely met with in the ordinary analysis, as a rule, we may dispense hunting for it.)

Precipitate under the Influence of Heat and of Nitric Acid.

What is the nature of this precipitate? Is it formed by globulin or by serin, or by both these albuminoid substances? Such are the questions to be resolved necessarily at the outset.

Globulin.—We should always begin by hunting for globulin. Its presence may be suspected when the urine is cloudy and does not clear on rest or on filtration, and especially when by the addition of water the cloudiness increases; but these

characteristics are far from sufficient to warrant us in affirming its presence.

To detect it three chemical procedures are at our disposal:

Pass a current of carbonic acid through urine containing globulin; at the expiration of three to four hours the urine becomes cloudy; at the end of one to two days (not always, however) a milk white precipitate forms which is redissolved on the addition of one per cent. chlorhydric acid and a few drops of marine salt.

This method is a very good one, but it is hardly adapted to clinical purposes.

Add a concentrated solution of chloride of sodium to the urine and a precipitate is formed if globulin is present.

This method has the advantage of being expeditious, but it has the disadvantage of giving no result when the amount of globulin is small.

The third method, that of Hammarsten,[60] is adopted uniformly, and in it the sulphate of magnesium is used.

We may proceed in two ways:

The urine is supersaturated with sulphate of magnesium, perfectly pure, and especially free from sulphate of iron; this salt being soluble in urine to an equal weight (80 per cent.), it should be dissolved by shaking until a final fragment remains undissolved. At the end of a few hours the globulin contracts into flocculent masses which need only to be filtered.

Add to a given quantity of urine (10 to 20 c.c.) an equal amount of a saturated solution of sulphate of magnesium (a few crystals should remain undissolved); then expose the mixture to cold for twenty-four hours. The globulin forms a coagulum which floats in the liquid or at the surface; rarely it precipitates to the bottom; the liquid may be decanted or filtered.

This method, which we habitually use, is very sensitive; it allows us to detect the slightest trace of globulin, even where the heat test reveals nothing in the urine.

Latterly Professor Ott,[61] of Prague, has said that when globulin is precipitated by the sulphate of magnesium, a portion of the serin is also thrown down if the urine contains a certain amount of acid phosphate (.5); therefore he recommends, with emphasis, that the urine be neutralized as much as is possible before the addition of the sulphate of magnesium.

To complete this question let us add that recently Pohl[62] recommends as a test for globulin the sulphate of ammonium, a test suggested some years before by Hofmeister; the following is the procedure:

Acid urines are neutralized with ammonia, and the deposited phosphates are filtered; we thus obtain what is essential —an alkaline urine. Add to this urine a saturated solution of sulphate of ammonia. In case globulin is present, at the end of an hour a precipitate is formed.

Although Pohl's method is much more rapid than Hammarsten's, we prefer the latter; it seems to us more reliable. In certain instances, indeed, we have thus detected globulin which the sulphate of ammonia had failed to reveal.

Serin.—Serin is sought for in the filtrate free from globulin; that this latter point may be assured special filter papers should be used (Berzélius's filters); if this precaution be neglected globulin, which is a ready dialysate, will remain in the filtrate.

In order to detect serin in the filtrate, one of the methods already spoken of may be employed;[63] if a cloudiness or a precipitate forms it is due to serin; it may be isolated by filtration.

The urine, thus successively tested, should be absolutely clear of globulin and of serin—that is to say, of all the albuminoid substances which are precipitable by the agents ordinarily used in the search for albumin.

To be certain of this, and to avoid all chance of ulterior error, control tests should be made. We have a number at our disposal to which we will briefly refer:

Acetic Solution of Ferrocyanide of Potassium.—The urine acidulated by acetic acid is kept in a water-bath for several hours. The albuminous coagulum having been filtered, an acetic solution of ferrocyanide of potassium is added, and the mixture is allowed to rest for two to three hours. If at the end of this time the urine is perfectly clear all the albumin has been eliminated. If, on the contrary, there is the least cloudiness, albumin is present.

In the latter event, it is necessary to begin over again, to boil again the urine acidulated by acetic acid, and then to test, as above, the filtrate by the acetic solution of ferrocyanide of potassium.

This method is very tedious, for usually we are obliged to

repeat it; further, in certain cases, where the urine is too acid, or where it is primarily alkaline, no result is obtained. We therefore only mention this method in order to reject it absolutely.

Concentrated Solution of Acetate of Soda.—This method, advocated by Hofmeister, is far superior to the preceding in rapidity; Professor Jaccoud recommends it in his lectures.

To a half litre of urine 10 c.c. of a concentrated solution of acetate of soda is added, then perchloride of iron, drop by drop, until the liquid presents a permanent blood-red color. Next boil until the iron precipitates as basic acetate carrying with it the coagulated albumin. Then filter and in the filtrate not a trace of albumin should remain.

If we are to believe Wasserman [64] this method is not always precise; if it be repeated in order to separate traces of albumin, this may be transformed into hemialbuminose and even into peptones.

Chloride of Sodium.—Salkowsky [65] and latterly Dumontiers [66] have lauded the following method:

Boil the urine previously acidified by acetic acid; add an excess of chloride of sodium; filter to clear the urine of the coagulated albumin.

This method, aside from its great simplicity, has the great merit of totally eliminating the albuminoids, as we have often pointed out; it is, therefore, the one which we have always used.

No Precipitate by Heat and Nitric Acid.—When there is no precipitate on heat or nitric acid, or rather when none forms, we should, after having resorted to one or another of the control tests enumerated, test the urine for peptones.

Many methods have been indicated with this end in view. Hofmeister ranks them under four; we divide them into two chief classes:

Methods for directly testing for peptones.

Methods for indirectly testing for peptones; that is to say, after precipitation.

Methods for Testing directly for Peptones.

These methods are simple enough, but unfortunately they are only precise when the peptones are present in definite amount, and when the urine is very slightly colored, or, better

still, colorless; although the latter condition is usually easy to meet, the same does not hold true of the former.

Whatever the case, we must proceed as follows:

Clear the urine of mucin and of albumin; then test the urine for peptones by Millon's reagent, or, preferably, by the reaction of bicyanate of ammonium.[67]

Millon's reagent, one of the most sensitive means for revealing the presence of all proteid bodies, whether in solution or not, is obtained as follows:

In concentrated azotic acid (density = 1.41, boiling point = 115 to 120°) dissolve mercury, at first by cold and then by gentle heat; at the end of an interval decant the clear liquid from the crystalline precipitate; the liquid thus obtained is Millon's reagent.

To use it add it to the suspected liquid and heat to 60° or 100°; if peptones be present we obtain a deep-red color which does not disappear on long contact with air or by protracted boiling; this color, much more accentuated than that produced by contact with other albuminoid substances, is absolutely essential for the affirmation of the presence of peptones (Maixner).

Far more preferable seems to us the *reaction du biuret*, bicyanate of ammonium test: add to the urine two drops of soda or of potass solution, and then a few drops of a two per cent. solution of sulphate of copper; if peptones are present, we obtain a coloration varying from violet-rose to purple-violet, when the proportion of peptone is considerable, although some writers claim that the shade of the color depends on the concentration of the solution and on the quantity of copper salt added to the liquid.[68]

This reaction, called *du biuret*, receives the name because the bicyanate of ammonium (*biuret*) acts in the same way in the presence of the same reagents; it occurs in the presence of other albuminoid matters, but the coloration is different; thus in a solution of serin a clear blue color is obtained.

Methods for indirectly Testing for Peptones.

In order to indirectly test for peptones—that is to say, after precipitation—alcohol, tannin and phosphotungstic acid may be used.

Aside from precipitation by alcohol, which is very defective, and precipitation by tannin, which requires too much time to be of value for current work, we will simply describe the method of precipitation by phosphotungstic acid:

Add to the urine $\frac{1}{10}$ of concentrated chlorhydric acid; next add a solution of chlorhydric of phosphotungstate of soda, the formula of which is:

Phosphotungstate of soda, . . .	25 gr.
Chlorhydric acid, ...	5 "
Distilled water, ...	250 "

until there is no further precipitate. Filter and wash the filtrate with water acidulated by sulphuric acid three to five per cent.; heat for a short time. The peptone dissolves in the water, and filter to get rid of the insoluble barytes; there remains a colorless watery solution of peptone which is subjected either to Millon's, or, better still, to the *biuret* reaction.

This method, which according to Hofmeister reveals 25 gr. of peptone in a litre of urine, has been used by von Jacksch in all his researches on peptonuria.[69]

After his experiments, Hofmeister[70] proved that the solution of chlorhydric of phosphotungstate of soda precipitated creatinin. He, therefore, advised the substitution of the acetic solution of phosphotungstate of soda; if, following this advice, we employ the latter, the urine must first be acidified by acetic acid. In using this method we may consider as peptones any precipitate forming within five minutes; only the peptones precipitate thus quickly.

In addition to this method, which allows of the recognition of even traces of peptones, but which has the disadvantage of requiring much time, there are others less sensitive but more rapid; they must hence be mentioned.

Picric Acid.—This method has been highly lauded by Johnson,[71] professor of clinical medicine. A saturated solution of picric acid precipitates peptones as well as serin and globulin; it is, however, easy enough to differentiate the precipitates. Heat them and filter while hot; the peptones are dissolved and pass with the filtrate, while albumin (serin and globulin) remain on the filter-paper. The filtrate, subjected to the *biuret* test, should in case of peptonuria, give a color varying from rose to violet-purple.

Tauret's Reagent.—Even as picric acid so does Tauret's reagent precipitate the three principal albuminoids of the urine; serin, globulin, peptones; similarly, also, the precipitates act differently according to circumstances; the albuminous precipitate (serin and globulin) increases by heat, the peptonic precipitate disappears. We proceed as follows:

Into a test tube pour the urine entirely freed from albumin, and then add a few drops of Tauret's reagent; in case peptones are present, a cloudiness or a whitish precipitate forms at once. Heat the tube and the liquid clears. Plunge the lower part of the tube into cold water and the precipitate reappears, but only in the chilled part.

This property of disappearing in heat and of reappearing in cold is also common to the precipitate formed by alkaloids; therefore we must always, before affirming the presence of peptones, be assured that the patient has not ingested any substance of this nature during the days preceding the examination. Notwithstanding, it is well to use control tests, in order to differentiate between peptones and alkaloids; and alcohol readily discolors the latter and is without much effect on the former. Tauret's reagent would be then an excellent one for revealing peptones if it did not precipitate other substances; creatinin, guanin, xanthine, pus, semen, epithelial *débris*[72]; nevertheless, it may be used but only by resorting to control tests.

Before finishing this second part of our chemical study, let me say a few words only on the test for hemi-albuminose.

The urine having been freed from albumin add a neutral salt to saturation, and acidify with acetic acid; a precipitate forms which, subjected to the influence of heat, disappears completely, but reappears on cooling.[73]

The Dosage of Urinary Albumins.

Now that we are familiar with the methods of recognizing albumin in the urine and of testing for the different varieties, we must for completeness' sake consider a final question: the dosage of the diverse urinary albumins.

Dosage of Albumin.—By means of the precipitate yielded by heat or by nitric acid we may at once form an approximate idea of the amount of albumin contained in the urine,

and consequently of the absolute amount if we know the quantity of urine secreted in twenty-four hours. In the strongly albuminous urines the precipitate is flocculent, it is furfuraceous in urines moderately charged with albumin, and simply molecular in those which contain only a feeble quantity of the coagulable element.

The measure of the volume of the coagulum does not give much more exact indications than the simple inspection of the precipitates at the time of their formation. The particles resulting from the coagulation of a urine poor in albumin precipitate more slowly and do not tend to cohere to any great degree; they always occupy, therefore, a greater space than the larger and heavier flocculi which cling more forcibly together, so that the differences in height are far from expressing the differences in weight of the precipitates. Further, in case of the same urine, the deposit will vary according to two circumstances:

The duration of the boiling: the albuminous masses running together and enlarging according to the length of time during which the specimen is boiled.

The interval of rest: during which the liquid can separate and the precipitate can condense.[74]

For purely approximative determinations, for example, where the physician wishes to know if albumin is present in scanty or in large amount, or further if this quantity enlarges or diminishes, we may follow the annexed very simple procedure:

Precipitate the urine, by heat or by nitric acid, in a test tube of the same diameter throughout, and let it settle for from twelve to twenty-four hours; we may then readily compare the volume of the precipitate with the quantity of urine taken for test. By keeping the precipitates taken each day we may readily compare the varying quantity of albumin and thus see whether it increase or diminish. This method of testing is all the more exact if we take graduated tubes of exactly the same volume.

By this procedure we estimate only the relative amount of albumin contained in the urine.

Further this method is always a trifle inexact. According to the specific gravity of the urine, according as under the influence of heat the albumin has precipitated in small or in large

particles, the albuminous coagulum occupies now a larger and now a smaller volume. Vogel,[75] comparing this method with that by weight, has found errors of from thirty to fifty per cent.

This simple method is therefore inexact enough, even for judging the approximate quantity of albumin, and its results are quite incomplete. Therefore in order to obtain results perfect enough for clinical purposes we must resort to the method of dosage.

Many procedures have been devised for this purpose; we will only mention the principal, insisting on those which seem to us to be of value clinically. To pass them even rapidly in review, it is necessary to class them in groups, and we adopt the classification of Professor Lépine,[76] to be found in his notes to Bartel's treatise on Diseases of the Kidneys.

Densimetrical Methods.—The methods recommended by Lang,[77] Höebler[78] and Bernhardt[79] are at first sight seductive enough; they aim at obtaining the specific weight of the urine before and after the coagulation of the albumin; but, since it is very difficult to remove all the precipitate, and nothing but the precipitate, the results are very inexact.

Methods of Dosage by Opacity.—The aim is to determine the degree of cloudiness given by the coagulation of the albumin; in order to well appreciate this it is necessary, generally, to dilute the urine notably with a certain quantity of distilled water. The methods advocated by Vogel[80] and by Potain[81] are applicable especially to urines containing but little albumin, and they are exact enough if we are to accept the control results of Vogel and Masing.[82]

Polarimetrical Methods.—Biot[83] and Bouchardat[84] first determined that albumin deviates the needle to the left 50°; and Becquerel[85] having found that the degree of deviation was proportionate to the concentration of the solution, proposed this method for the dosage of albumin; according to him each degree will correspond to 18 centigrammes of albumin.

Although this method is excellent for determining the amount of albumin in water it is far from giving as good results in an albuminous urine; the coloration, the greater or less cloudiness interfere with the examination; the presence of salines renders equivocal the quantitative valuation of the

albumin; and therefore we often find quite great disagreement between the scales and the polarimeter.[86]

Methods of Dosage by Standard Solutions.—The best known is that of Bodeker,[87] which gives very good approximate results; and the same holds true of Tauret's[88] method, which is more rapid in its results.

Methods of Dilution.—These methods are based on the fact that if the quantity of albumin is very slight, and nitric acid be added with care, the albumin ring only appears after the lapse of some minutes.

Roberts[89] and Stolinkoff[90] dilute the urine by degrees until the albumin ring only appears at the end of about forty seconds. Brandberg[91] follows the same course, only he dilutes more, so that the ring only appears at the end of three to four minutes.

The method of Musculus[92] is somewhat different; instead of varying the dilution of the urine he takes account of the variable time required by the albumin ring in forming in a urine diluted enough to require a certain time before this ring should form. This writer has prepared a table which may be consulted to determine at once the richness in albumin of the urine examined. Here are a few of the figures:

Quantity of Albumin to the Litre.	Beginning of the ring.	Ring well formed.
0 gr. 20	at once	½ minute
0 gr. 10	½ minute	1 "
0 gr. 05	1 minute	2½ minutes
0 gr. 01	7 minutes	15 "

This method, which is attractive enough, has been used several times by Professor Lépine who was not specially pleased with it; it is hardly likely that it can be used clinically.

Method of Redissolution.—This method has very lately been advocated by Dr. Luton[93] of Reims.

By means of heat the albumin in a known quantity of urine is coagulated, and it is then redissolved by a standard solution of tartaric acid.

Up to now Dr. Luton has only been able to obtain relative results; he hopes, however, in the future, to obtain absolute results—that is to say, to determine the exact weight of albumin contained in each litre of urine.

Method by Weight.—Weight in the dry state of the coagulated albumin is without question the most exact method of dosage; on this point all chemists are in agreement, only differing in regard to the substance to be used for coagulating the albumin.

Some prefer heat, the urine having been first acidified by acetic acid; others alcohol; in the first instance precipitation is incomplete; in the second other substances are precipitated at the same time as the albumin. This is the reason why Méhu[94] recommended phenic acid; this acid combining with albumin, we are exposed to an error which may reach sixteen per cent. Esbach,[95] who determined this point, rejects this acid absolutely, and recommends precipitation of the albumin by picric acid; the picrate of albumin thus obtained is weighed and the weight is multiplied by .8. In order to place this method above reproach it is necessary (and this is by no means proved) that the albumin and the picric acid should always combine in the same proportion.

An excellent and rapid method is for certain chemists the bi-chloride of mercury, but this salt unfortunately precipitates in part the peptones.

Whatever the coagulating substance used this method is liable to errors which we must remember if we desire to obtain exact dosage; further it takes time and great care. It seems to us, therefore, scarcely adapted to clinical purposes, and this is the reason why we do not describe it at length.

Methods by Deposit.—There remain to be considered the methods which consist in measuring the weight of the albuminous deposit in a tube where the albumin is precipitated always from the same quantity of urine.

Although the method is about identical in all the instances, it is not in regard to the coagulating agent used; nitric acid,[96] phenic acid,[97] picric acid,[98] these agents have been recommended; the latter, in particular, especially as recently modified by Esbach, seems to give excellent results. We will, therefore, describe it somewhat at length; and it is the method ordinarily resorted to.

The following is the principle on which it is based:

In a graduated tube the albuminous urine is treated in a cold solution of citro-picric acid; after an interval of rest read the height which the coagulum attains. Since the graduation

of the tube represents in grammes the amount of albumin contained in a litre of urine, we know at once the amount of albumin in the specimen examined.

Special reagents and graduated glass tubes are two elements necessary. We will say a few words of these:

To obtain the reagent, proceed as follows:

In 600 to 800 gr. of water, dissolve by heat 10 gr. picric acid and 20 gr. citric acid, pure and dried in the air; on solution add a quantity of water sufficient to make a litre, such is the citro-picric reagent (modified) of Esbach. (Picric acid precipitates albumin, while citric acid keeps the phosphates and the urates in solution.)

The graduated tubes are .15 cent. in height and .015 millim. and $\frac{1}{2}$ interior diameter. Above the line of grammes is marked a U, and higher up an R.

Proceed as follows:

Add the urine up to the U, and the reagent up to R, stop the tube with the thumb and turn the tube twelve times without shaking (each turn including the inversion and re-inversion of the tube). Close with a rubber cork and allow to rest for twenty-four hours. At the end of this interval, read the height of the coagulum, at the centre of the albuminous surface, which is ordinarily more depressed than the borders. In order to obtain satisfactory results by this method it is essential:

The Urine must be Acid.—Since albuminous urines undergo more rapidly than others ammoniacal fermentation, we must always assure ourselves by test paper of the acidity of the specimen. It must give a strong acid reaction.

The urine must not be too rich in albumin. If the urine appear too rich add one to two volumes of water, not exceeding four grammes total amount; take this dilution later into account by doubling or triplicating the obtained reading.

This method, say Neubauer and Vogel, is very simple, does not require much time, and gives exact enough clinical results.[99]

Guttmann[100] in a recent article reaches the same conclusion. He says: "Owing to the results obtained from Esbach's method, which are nearly as exact as those yielded by weighing the dried coagulated albumin, and owing to its ease of application, I cannot too highly endorse it."

The method of Esbach is, however, liable to error; it may yield a precipitate when there is not a trace of albumin in the

urine; this fact has recently been noted by Dr. Kuthe[101] and by Teil (of Holland) in a letter addressed to our teacher, Dr. Dujardin-Beaumetz, and we reproduce the criticism here:

In a patient taking the sulphate of quinine in quite large dose, Dr. Kuthe found by Esbach's tube a manifest precipitate, while he obtained none by the ordinary reagents. Supposing this precipitate to be due to the sulphate of quinine, he suppressed it and the precipitate could no longer be obtained; it was due then to the formation of the picrate of quinine.

This fact it is important to note; we must bear it in mind when examining the urine of patients taking quinine. In doubtful cases, we may readily enough differentiate the quinine precipitate from an albumin coagulum; the first disappears by heat, while the second persists.

We may conclude, then, that although Esbach's method does not suffice to determine traces of albumin, it allows us to follow efficiently the daily variations in amount; and it is hence of signal value in the routine examination of the urine of Bright's disease.

Dosage of the different Kinds of Urinary Albumin.

The dosage of albumin as an entity being such a relatively complex affair, when we desire perfectly exact results, it is readily apparent how much more difficult is the separate dosage of the different kinds of albumin; we will, therefore, deal briefly with this part of the subject, seeing, also, that it is as yet hardly fit for clinical purposes.

Globulin and Serin.—We will describe in his own words the method devised by Professor Lépine,[102] who has specially studied these substances:

"50 to 100 c.c. of filtered urine are mixed with an excess of sulphate of magnesium and allowed to rest; at the end of an interval small flocculi appear in the urine. Pour through a filter paper, the weight of which is known, and wash the precipitate with a cold saturated solution of sulphate of magnesium. The filter paper and the precipitate are inserted into a vessel with a small quantity of water and shaken during a period sufficient to reduce the paper to a pulp. The contents are next poured into a porcelain capsule, in order to render insoluble the globulin, which has been partially, perhaps entirely,

redissolved in the water; boil and pour on a filter paper, wash with boiling water, dry at 100°, and weigh with the usual precautions; deducting the total weight from that of the first filter paper we obtain the weight of the globulin. To obtain that of the serin, we use the first filtrate which has been freed from globulin; acidify it slightly, boil, recover the precipitate on a filter, wash with boiling water, dry and weigh."

Our object in entering into the details of this method of Lépine has been to prove its difficulties. Such a method is not at all applicable clinically; too much time is required, the manipulations are of too delicate a nature for routine purposes.

For this reason we prefer a method less complex, which allows us to differentiate the weight of the globulin. We proceed as follows:

Divide the filtered and acidified urine, which has been freed from mucin, into two parts.

Treat the first part by the citro-picric reagent in an Esbach tube; on the following day we know the total quantity of albumin, that is to say, the amount of serin and of globulin combined.

To the second part is added a saturated solution of sulphate of magnesium; on the following day globulin, if present, is precipitated; filter. The filtrate, containing only serin, is poured into an Esbach tube and the citro-picric reagent is added. In twenty-four hours a coagulum is obtained which represents the amount of serin by multiplying by two the figure obtained, since the liquid acted on the second time is a first dilution of the urine; it is, in fact, composed of half urine and half saturated solution of sulphate of magnesium.

Deducting the weight of serin from the total weight of the serin and the globulin we obtain the amount of globulin.

Such is our method; although the results are not pefectly exact, and this we readily grant, they are at least enough so to allow of comparison from day to day; the method is simple and clinically applicable to routine purposes.

Peptones.—Up to now we are satisfied with determining the presence of peptones; no one has as yet proposed a method of dosage. We have had no personal experience and therefore will not dwell upon the subject.

Method of Examining an Albuminous Urine.

Before ending these chemical considerations, we must state the steps we have followed in our various researches.

1. We first filter the suspected urine; if, after filtration, it is cloudy, we add a little acetic acid to precipitate the mucin; at the end of a few minutes this is filtered off.

2. We next verify the reaction of the urine; if it is not sufficiently acid—that is, if it does not redden litmus paper markedly—we add a few drops of acetic acid.

3. A part of the acidified urine is then subjected to heat or to nitric acid, to find out whether it precipitates or not:

In the first instance we seek the nature of the precipitate: To 10 or 20 c.c. of urine, rendered neutral, we add a saturated solution of sulphate of magnesium; at the end of twenty-four hours we obtain or not a precipitate or cloudiness which we filter. In the filtrate, which is deprived of globulin, we seek for serin by one of the methods we have mentioned.

In the second case, that is to say when no precipitate forms, we resort to a control test to eliminate the albumin (serin and globulin); these are completely separated by the chloride of sodium. We then seek for peptones by the biuret reaction, after having first precipitated them by the acetic solution of phosphotungstate of soda.

4. The remainder of the urine is subjected to Esbach's method; the first test gives us the total amount of albumin, that is, of globulin and serin. The globulin having been precipitated by the sulphate of magnesium and filtered, we test the filtrate again by Esbach's method; the obtained figure, multiplied by two (since the urine has been diluted once), represents the quantity of serin.

The difference between the figures obtained by these two procedures represent the amount of globulin.

We believe that these methods of determination of the albuminoid substances, although only approximate, are exact enough for clinical purposes; they allow us to take account of the daily variations of the globulin and the serin in the same patient.

5. We complete our analysis by noting:

a. The quantity of urine; *b*. The density of the urine; *c*. The amount of urea, calculating this only after the elimination of the albuminoids, which otherwise might lead to error.

Such are the methods, unfortunately rather tedious, to which we must resort in order to make a complete examination of an albuminous urine.

We thus only obtain approximate results, however, but sufficient clinically, for, as M. Gubler says:

"Clinically, absolute exactness is not indispensable."

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CHAPTER II.

THE DIAGNOSTIC VALUE OF THE SYMPTOM ALBUMINURIA, IN BRIGHT'S DISEASE.

Before passing to the clinical side of this question we believe it useful to recall in a historical way the various phases through which this interesting question of albuminuria has passed. This digression appears to us a proper introduction to this chapter; it shows us, in fact, what was formerly considered the value of albuminuria, and it impresses on us what ought to-day to be its value.

Historical Considerations.

Discovery of Albuminuria.—Cotugno[1] first in 1770 determined that certain dropsical patients eliminated non-bloody urine which, when subjected to heat, gave rise to a coagulum similar to coagulated white of egg.

This discovery of Cotugno's was thirty years afterwards completely confirmed by the researches of certain English physicians: Cruiksank, Wells and Blackhall. Cruiksank[2] in 1798 based on the presence of albumin in the urine the principle of his classification of dropsies, dividing them into two chief classes: Albuminous dropsies, of general origin, and non-albuminous dropsies of visceral origin. This division was soon approved by his two compatriots. Wells[3] sometimes found at autopsy on individuals, who during life had had albumin in the urine, special alterations of the kidneys: "kidneys harder, with thickening of the cortex, alteration of the structure from the deposit of coagulable lymph, etc." He determined only the fact without drawing any deduction: "I do not thence conclude," he says, "that the kidneys are always diseased, when the urine contains much serum."

Blackhall[4] observed in an unusual proportion of cases renal lesions in dropsical and albuminuric individuals, but, doubtless

influenced by the alterations which he found both in the serous membranes and in other parts of the body, he saw in these diverse lesions the result of a general affection of an inflammatory nature. Indeed, while recognizing the validity of the observation of his predecessors, he was unable to determine the origin which remained unknown up to the well-known researches of Richard Bright.

Albuminuria and Bright's Disease.—The origin of albuminuria, Bright,[5] with reason, traced to affections of the kidneys, and he described very thoroughly the disease which bears his name. Before his day, as we have seen, it was known that dropsy was often associated with diseases of the kidney, and it was also known that certain dropsical patients had albuminous urine, but the frequent coexistence of dropsy and albuminuria with renal disease had never been insisted upon; this fact Bright established in the clearest possible manner in his first volume,[6] published in 1827. After having described the different causes of dropsy[7] he announces that dropsy may be due to a further cause, a special alteration of the kidneys, on which he dwells somewhat at length, and he adds that whenever dropsy depends on these alterations, the urine is more or less albuminous, while he has never found it coagulable in a large number of other cases of dropsy which he has examined. Convinced of the great importance of the examination of the urine in this new class of dropsies, he had the happy idea of invoking the collaboration of Dr. Bostock,[8] well known from his important physiological and chemico-pathological works. The latter (his experiments are related in Bright's work) determined a fact fully verified at least in great part, that in this new form of dropsy—

The urine always contains albumin, generally in considerable proportion, varying, however, according to the case.

The specific gravity is notably diminished. The proportion of urea and of salts sustains equally in all the cases a more or less pronounced diminution.

Bright's views were soon sustained in England by Christison[9] and Gregory.[10] Basing their views on numerous experiments these two writers concluded that we always find post-mortem renal affections in patients who during life presented albuminous urines.

A few years later, in France, Martin-Solon,[11] notwithstand-

ing the numerous facts noted by his contemporaries showing the diverse origin of albuminuria, defended the ideas of Bright, of Christison and of Gregory. In his book (1838) on albuminuria, he described various affections, independent of Bright's disease, but having the common characteristic of albumin in the urine.

Few authorities, it is true, accepted these ideas; they adopted, the majority at least, those which two years later Rayer promulgated in his excellent treatise on diseases of the kidneys.

Albuminuria as a Symptom.—Already, before the appearance of this French work, opposition had appeared to Bright's views.

In 1832, Spittal,[12] in his inaugural thesis at Edinburgh, while granting the views of the distinguished physician to Guy's Hospital and his successors, stated that they were a trifle too absolute, and that the presence of albumin was not always a certain sign of the renal changes described by Bright.

A year later there appeared in France by direction of Rayer, the first work on this question, the thesis of Dr. Tissot,[13] "On Dropsy caused by Granular Affection of the Kidneys;" he determined that the presence of albumin in the urine is a sign of great value in Bright's disease, but he does not grant it absolute value, for he had found albumin in many affections to which he briefly refers. This thesis was the starting-point of many writings, instigated largely by Rayer. The determination of albumin became a matter of routine in the hospitals of Paris, and soon there arose striking differences in the observations.

Some writers accepted as proved in their entirety the ideas of Bright; for them Bright's disease and albuminuria were synonyms; Martin-Solon (to whom we have referred) personifies this school, which, notwithstanding the facts, for many years had but few adherents.

Others, having found albumin in cases where post-mortem the lesions described by Bright were absent, and also in patients not at all dropsical, concluded that the presence of albumin was absolutely of no value, or at least of very little value, since albuminous urines were met with in many diseases different both in seat and in nature.

Others, finally, and the great majority it must be confessed,

while admitting that albumin was found in other affections, considered albuminuria as a good sign of Bright's disease, but claimed that the symptom did not alone carry weight, but must be associated with other precedent or accompanying symptoms. This was the keynote of Desir's treatise (1835): "On the Presence of Albumin in the Urine as a Phenomenon and a Sign of Disease." This was followed two years afterwards by the letters of Forget, Professor of Clinical Medicine at the Faculty of Strassburg, letters addressed to Rayer and published in the *Gazette Médicale de Paris.* We reproduce the following extract, which seems to us to give an exact enough idea of the state of the question at this period:

"In how far does the art of diagnosis possess unequivocal, infallible, pathognomonic signs, in a word? Now what holds true for other diseases, does for albuminuria; after having pretended that the symptom uniformly meant an affection of the kidneys, the cases will be specified and emphasized which are exceptions, as in case of every other symptom, but the fundamental fact will remain established even though it be not infallible, and science will still be able to record a precious victory."[14]

The same opinion was expressed by Bouillaud[15] and by Rayer, in his superb treatise on diseases of the kidneys;[16] in England by Ellioston,[17] by Graves,[18] by Copland.[19] Bright himself[20] recognized this fact; he rejected the exaggerations of his successors, and claimed that he had never completely identified albuminuria with renal lesion.

Although Rayer's views were not at once accepted by all, they were rapidly enough in the years following the appearance of his treatise, years during which numerous theses and important works endeavored to determine the different cases in which albumin might be found in the urine, and to specify the value of the symptom albuminuria.

Albuminuria as a symptom was then an established fact, and it is no wonder that the Faculté required as a thesis for the degree of doctor in medicine: "The symptomatic value of albuminuria." Montanier,[21] chosen to sustain this thesis, begins in the following striking words:

"Some writers have made the word albuminuria a synonym for Bright's disease, for albuminous nephritis; this error has not gained ground, and to-day for everybody the word albu-

minuria represents a symptom common to a variety of affections; this symptom is the passage of albumin, or, better still, of the serum of the blood into the urine."

Since that time albuminuria has ever been regarded as a symptom, but the number of affections in which albuminous urine has been found has greatly increased.

Albuminuria in Health.—The presence of albumin in the urine of perfectly healthy individuals was discovered by Bostock (Bright's work) in 1827, and was confirmed by Spittal (Th. Edinb.) in 1832; in his inaugural thesis, previously referred to, he affirms on the authority of Turner and de Gmelin, that albumin exists in healthy urine, since it may be precipitated by tannin and the bi-chloride of mercury.

Notwithstanding, this question was neglected for many years; only lately was it reconsidered, first in England and in Germany, and next in France.

Vogel [22] and Ultzmann [23] reported cases of albuminuria in perfectly healthy subjects, but it is Leube [24] who first studied physiological albuminuria; he examined the urine of 119 soldiers in active service and in good health, at different times of the day, in the morning, in the afternoon, after a long march, and at night, and he found:

5 times albumin in the morning (4 per cent.)
19 " " " afternoon (19 ")
Never albumin at night.

The quantity of albumin found was further never considerable, never exceeding one per cent.

Gull [25] and Dukes [26] made about the same time analogous experiments on infants in England; they obtained the same results as the German writers. The same holds true of Moxon [27] who found the facts holding in particular for anemic and debilitated infants.

In France, Lépine [28] who first turned his attention to this question, proved that in a large number of patients albumin was found, at certain hours of the day, even in rather large proportions; and he thence concluded that albuminuria should only be considered pathological when present in large amount and associated with deterioration of the general health. Soon after Capitan [29] and de La Celle de Chateaubourg [30] confirmed the frequency of this physiological albumi-

nuria (in 700 samples of urine the latter found albumin in notable amount in 592 cases), and proved the variations from day to day.

Recently, Senator,[31] in his excellent study of albuminuria, has admitted—a fact, however, also proved by Possner[32] and Noorden[33]—that all normal urine contains serum albumin, but in rather small amount ($\frac{1}{2}$ milligramme to the litre, according to Possner).

Although this fact, determined by Senator, is of slight importance, since such a small quantity is not determinable by the ordinary reagents, the same does not hold true of the facts determined by Lépine, Capitan, and de La Celle de Chateaubourg. In all the observations of these writers we find appreciable amounts of albumin in patients presenting all the characteristics of perfect health.

From what has gone before, then, there results the following positive fact: side by side with pathological albuminuria there exists a physiological albuminuria which deserves serious consideration.

Bright's Disease without Albuminuria.—The presence of albuminous urine in many and in diverse affections had considerably diminished the value of this symptom in Bright's disease; the frequency of albuminuria in patients in perfect health had contributed still further to diminish this value; nevertheless, albuminuria remained one of the diagnostic signs of Bright's disease. If albuminuria could exist without Bright's disease it seemed impossible that Bright's disease should exist without albuminuria.

This fact is to-day, however, perfectly established, although by rather recent research. It was, if we are not in error, first called attention to in the thesis of Dr. Mozian:[34]

"Bright has the merit of having established the narrow corelation existing between the special lesion of the kidneys with albuminuria and the development of dropsies. Does it follow that these three phenomena form a species of trinity, one and indivisible? No, assuredly not. Ulterior observations have modified our ideas; dropsy may be lacking, and albuminuria, although constant, so far at least, in the renal lesion of Bright's, may be found under quite different circumstances."

A few years later Dr. Hue,[35] in his inaugural thesis is more explicit; he thus expresses himself:

"Whenever at autopsy we meet these anatomical lesions of the kidneys, we are sure that, during life, the urine has contained, for a greater or less time, albumin in greater or in less amount.

"Monneret and Graves have each reported a case in which the kidneys presented all the lesions of Bright's disease, and yet the urine had never offered the slightest trace of albumin. Since then, Mazomer, a Russian physician, has reported three additional observations of Bright's disease without albuminuria. We must admit that if many similar cases are recorded, albuminuria as a symptom will lose much of its importance. But such cases are exceptional.

"Are we not justified in asking if there be not erroneous interpretation, or if these cases may not enter into the following category: When we carefully follow the progress of Bright's disease, and we examine the urine each day, it frequently enough happens that, during a longer or a shorter time, and even several times during the course of the disease, no precipitate is obtained either by heat or by nitric acid. We may thus daily follow the diminution of the albumin, up to its complete disappearance, and then, after a variable time, it reappears gradually or very quickly.

"We see then that Bright's disease may exist without albumin being present in the urine; but this is dependent on the fact that the disease was not watched long enough. Whenever albuminuria is present and persists there is, without question, Bright's disease, but this may persist without albuminuria; it seems to us that the cases, of Monneret, Graves and Mazomer may readily be classed in this category."

We have made this long extract from Hue's work because it shows us well the state of the question at this period; it gives us also a just enough explanation of the fact. Still the possibility of Bright's disease pursuing its course without albumin in the urine was for long considered an anomaly. Of late years we find the question again studied. In 1874, Huchard,[36] in an article entitled "Quelques considerations sur les nèphrites latentes," insists particularly on this point—that nephritis, especially the interstitial form, may run a latent course; edema and albuminuria may be lacking, and the chronic inflammation of the kidneys may be accompanied only by persistent anemia, loss of flesh, digestive disorders, and special troubles of the intellectual faculties.

Lecorché[37] holds the same opinion; he recognizes the fact that in interstitial nephritis the urine does not necessarily contain albumin, and that this form of disease may pursue its course without our ever finding a trace.

The English and American writers are still more explicit:

Johnson[38] first studied this question, and he was followed by Mohamed; in a paper read before the London Congress (1881) and published *in extenso* in Guy's hospital reports,[39] the latter reports the cases of nephritis treated at Guy's hospital during 1879-1880; of 61 cases in 41 albumin was never found, and in 11 only at infrequent intervals. 21 of these cases died, and in all, post-mortem, renal lesions were found.

Therefore, according to him, neither albuminuria nor dropsy exist habitually, in chronic Bright's disease; when these symptoms appear they are the indices of acute or epithelial alterations.

The following year (1882) the same ideas were sustained by Millard in the New York Medical Journal: "On the Exclusion of Albumin in the Diagnosis of Interstitial Nephritis."

Soon in France the question was specially studied, first by Dr. Delespierre and then by our accomplished teacher, Professor Dieulafoy. In 1884 Delespierre[40] wrote in his inaugural thesis the following words:

"Albuminuria cannot be considered as a constant symptom in nephritis; often enough it may be wanting, and yet the clinician may find in the symptoms of the disease the elements for certain diagnosis."

More recently Professor Dieulafoy, who has for long studied specially the diseases of the kidneys, read before the *Société médicales des hôpitaux* (June 11, 1886) the report of four convincing cases in which he was able for a greater or less time to determine the complete absence of albumin, although many symptoms of Bright's were present, and ultimately autopsy proved disease of the kidneys. A few months later (October 22, 1886), in a second paper, he presented to the academy three further cases of Bright's without albuminuria. Finally, very recently, in his lectures at the School of Medicine, he has laid special stress on these cases of Bright's disease without albuminuria which it is so important to recognize. We have often personally during our term of service had the opportunity to testify to the exact researches of our teacher.

The fact, then, is perfectly established to-day that Bright's disease may exist without, during life, albumin being detected in the urine.

To resume, then, the history of this affection in a few words:

Albuminuria, first considered a symptom of but little importance, and as an anomaly, gradually became the pathognomonic sign of Bright's disease to such a degree that certain clinicians considered albuminuria synonymous with Bright's disease.

Next, numerous observers, having found albuminous urine in many and in diverse affections independently of all renal lesion, and again having found albumin in the urine of subjects enjoying the most perfect health, albuminuria became a symptom common to many diseases. This symptom, the absolute value of which has certainly diminished, has still, however, great weight in the diagnosis of Bright's disease. When a number of symptoms suggest the possibility of a chronic renal affection, albuminuria remains the great diagnostic criterium; the affection remains doubtful if this symptom be lacking, and it becomes certain if this symptom appears.

Finally, it became a certain fact that Bright's disease may exist for a greater or less time, perhaps for a life-time, without albuminuria; the symptom thus loses much of its diagnostic weight. If its presence (under certain conditions) still indicates truly a renal affection, its absence does not entitle us to reject the affection, and the diagnosis of Bright's disease may be made even when the most sensitive reactions do not allow us to discover the slightest trace of albumin in the urine.

Diagnostic Value.

Albuminuria, an unquestioned fact to-day, has lost to a great degree its old-time diagnostic value.

Does it still possess value? If so, to what degree? These are the questions we aim at answering.

We will begin by establishing the indications we are justified in drawing from the presence or the absence of this symptom.

We will next see if the physical and chemical nature of albuminuria can give us information in regard to its origin and its cause.

We will then examine if it is possible to draw the relations which exist between the presence of albumin in the urine and the urinary secretion,—considerations of interest in regard to the lesion.

We will conclude by seeking if there exist between albuminuria and the various symptoms presented by the patient, relations which will help us in affirming the presence of Bright's disease.

Having passed all these questions in review, we trust we will be in a position to answer the first question of our research:

What is the diagnostic value of albuminuria in Bright's disease?

The Existence of Albuminuria.—We cannot examine this question of the presence of albuminuria in its entirety; for the sake of ease of description certain divisions are essential; we must take clinical types; those with which we meet most frequently may be readily classed under the following three heads:

Parenchymatous nephritis.
Interstitial nephritis.
Mixed—or, better still, diffuse nephritis.

Although, as has been with justice emphasized by Dieulafoy, it is this latter form which is met with usually, we will dwell at greater length on parenchymatous and on interstitial nephritis, because they present more marked characteristics.

Parenchymatous Nephritis. — Albuminous nephritis (Rayer); epithelial nephritis (Lancereaux); tubular nephritis (Dickinson); non-desquamative nephritis (Johnson); large white kidney (Bright's kidney).

Presence of Albumin.—The capital alteration of the urine in this variety is the presence of albumin. This is of such importance that since Bright's day the determination of chronic albuminuria is considered the best sign of a renal affection; and since Rayer's time many writers have called the affection after him albuminous nephritis—a happy enough name, we must grant, for in the great majority of cases not only is albumin present but it constitutes one of the chief if not the principal symptom of this affection.

The quantity of albumin secreted by the kidneys in parenchymatous disease is usually considerable. Generally it con-

tains from 5 to 8 grammes albumin according to Rendu, from 6 to 12 according to Lecorché; frequently enough the proportion rises to 15 to 20 grammes in the twenty-four hours. Rarely does it exceed this figure; still, Bartels has cited a number of cases where the amount of albumin surpassed 5 per cent.; more rare are the cases where the amount is as low as 1 to 2 grammes to the litre.

Aside from these variations there are others most interesting, which may be noted when account is taken of the daily progress of parenchymatous nephritis. These variations are of two sorts: the first are related to the period of the disease, and the second occur suddenly from day to day; we will dwell a trifle on each variety.

It is an established fact that the quantity of albumin varies during the course of a parenchymatous nephritis. But do these variations coincide constantly with a given period of the disease? An affirmative answer seems to us *à priori* improbable. A cursory glance through the literature of the subject will teach us what slight accord in opinion there is on this point.

Christison[41] first noted that it was during the initial period of the affection that the quantity of albumin reached its maximum; Lecorché[42] accorded with this view. Rayer[43] believes that albumin increases with the progress of the disease. Bartels[44] categorically establishes this; "it is at the acme of the disease, he writes, that this substance is present in greater quantity than at other times."

It should be stated that the majority of writers are in accord in regard to the fact that it is in the last stage of the disease—that of renal atrophy—that the amount of albumin is least considerable; at this stage the decrease may extend even to complete disappearance.

In the same patient, further, albumin may diminish from day to day; these daily variations ordinarily coincide with the variations in the quantity and the specific gravity of the urine. They are in quite constant relation with the density and in inverse relation to the quantity of urine eliminated each day. These changes are not accompanied by any alteration in the health of the patient, and they occur without known cause. An increase or a decrease in the quantity of albumin does not indicate an amelioration or an aggravation of the disease.

This point we must insist upon, for it is not as yet generally recognized.

Absence of Albumin.—"It may happen that the albumin disappears even at the end of the disease, but from time to time, up to death, we see it reappear under the influence of various causes." Jaccoud is still more categorical: "The absence of albumin is even the rule in the last period of the disease." Although the majority of writers are not in accord in regard to the frequency of the disappearance of albumin during the last stage, the greater number admit at least the possibility on the occurrence of renal atrophy: there is far less agreement in regard to the possibility of disappearance during the course of a parenchymatous nephritis.

"Frerichs, Bright, Christison, Mahmsten, Johnson, have reported cases where, the albuminuria ceasing, the parenchymatous nephritis still persisted. We cannot *à priori* accept these cases, since albuminuria for us constitutes the pathognomic sign of intra-canalicular inflammation; it may happen, however, that the albumin diminishes, and even disappears."

Jaccoud[45] is less affirmative: "At this stage the albumin may disappear for a few days and then return later."

In case of the large white kidney, then, it seems to us that there may occur transient disappearance of the albumin lasting for some days, or even for some months.

I report the following case, which we met with the current year.

Case I. (*Personal.*)

Bright's Disease (*Parenchymatous Form*). *Transient Disappearance of the Albumin.*—M——, æt. forty-seven, was admitted to the Necker Hospital, February 23, 1887, service of Professor Dieulafoy.

The man had had typhoid fever at the age of seventeen; in the month of August, 1886, as the result of catching cold, he had had chills, fever, nausea, bilious retching, pain over the kidneys lasting for two to three days. Soon after there appeared headache, intense dyspnea and nocturnal cramps. These symptoms lasted till October 15; then they became exaggerated and in addition there was swelling of the eyelids, edema of the feet and legs up to the knee, buzzing in the ears, slight deafness, etc. These symptoms caused the man to cease work; he entered the Beaujon Hospital November 10, 1887. While there he suffered from polykiuria with polyuria (1500

gramme daily), and albumin appeared. On January 19 he felt relieved, left the hospital, and resumed his work.

This condition lasted till the middle of February. Then the chill and fever recurred, as well as the other symptoms. He then entered our service at the Necker.

The dyspnea was then intense, especially at night, numerous bronchial râles were scattered over the lungs, the edema was almost generalized. There was no albumin in the urine. The man was placed on milk diet and a mixture of syr. of ether and of syr. of orange flowers was prescribed.

February 24, urine acid, 1.200 c.c.; no albumin.

February 25, urine alkaline, 800 c.c. no albumin.

February 26, urine acid, clear, 1.750 c.c., no albumin. The dyspnea has diminished but the man feels no better.

February 27, urine slightly acid, sediment, 1.000 c.c., a trace of albumin. The man feels worse; chill; backache, nausea, bilious vomiting.

February 28. Trace of albumin persists; dyspnea exaggerated, numerous râles in the lungs.

March 1, alkaline urine, 400 c.c.: properly tested it yields albumin 14 grammes to the litre. On his body there appeared a vesiculo-pustular eruption; the diagnosis of varioloid was made; at the end of two weeks he was cured, and he was discharged on April 15.

Time and again the examined urine contained albumin. The man returned to work and continued till May 10. He then caught cold, had chills, pain in the loins, the urine became scanty, and micturition was frequent. He remained at home for several days under ordinary diet. The symptoms increased, the edema returned, and he entered the hospital again on May 18, 1887.

May 19, the urine is cloudy, scanty, and contains .75 grammes of albumin (serin).

He remained in the hospital for several months; his urine, examined daily, varied from 1.000 c.c. to 1.600 c.c., and always contained from .25 to .75 gramme albumin (serin).

From June 10 the symptoms disappeared under continuous milk diet; the urine became normal and contained no albumin. Twelve days after he returned home and we have since lost sight of him.

This case is of interest, for it proves clearly that in the course of a parenchymatous nephritis, the albumin may transitorily disappear.

From the 23d to the 27th of February it was absolutely lacking, and then reappeared.

Did this happen only under the influence of the renal affection? Did not the general intercurrent affection have an influence?

During the second stay of our patient in the hospital, we found for twenty-two days albumin in the urine; it then disappeared and there existed no trace during the last twelve days he was with us. Likely enough the treatment caused this disappearance. To resume: in this man, on two different occasions, albumin was lacking; although we can readily explain the second disappearance it is not easy to account for the first.

Do there occur cases where during the whole course of the disease albumin is lacking? We do not believe that this is possible, and we find no such record anywhere. We must except Henoch's case; here albumin was absent during the whole course of the affection, verified post-mortem; it only appeared the evening before death. We give a short analysis of the case:

CASE II. (*Abstract.*)

Scarlatina.—Acute parenchymatous Nephritis; no Albuminuria.—Death.—Autopsy.—A young boy of twelve was admitted into the service for children at the Berlin Charité on July 22, 1873. The face and scrotum were edematous and had been for several days; he was desquamating from scarlet fever of three weeks previously. The urine was red, very acid, no albumin; in the sediment there was present microscopically no element suggesting nephritis.

On the 23d and 24th the edema increased, but there was no change in the urine. The night of the 24th violent attacks of eclampsia occurred, with complete loss of consciousness.

The morning of the 25th delirium and cyanosis; by catheter a small amount of urine was obtained containing a large amount of albumin, and numerous hyalin casts.

The morning of the 26th consciousness returned; persistent cyanosis, dyspnea, imperceptible pulse, dullness at the base of both lungs, fine râles. Death the morning of the 27th.

At autopsy: Parenchymatous nephritis on both sides; serous effusion into peritoneum, pericardium, pleural cavities; edema of lungs, etc.

Such as far as we know is the only recorded case of parenchymatous nephritis without albuminuria—at least, throughout the greater part of its existence. This case we insist, however, has reference to an acute parenchymatous nephritis, and is therefore different from the affection we are now studying.

To resume, then:

Albumin is present in chronic parenchymatous nephritis.

The quantity, generally considerable, varies according to the individual, but in the same patient according to the period of the disease; it varies from day to day, and this too without alteration in the state of the patient.

Albumin may be lacking in chronic parenchymatous nephritis; this is not unusual in the last stage, but may occur in the course of the disease at longer or shorter intervals; never, up to now, however, has a parenchymatous nephritis progressed without albuminuria.

Interstitial Nephritis.—Hyperplasic nephritis (Lecorché); diffuse primitive proliferative nephritis (Lancereaux); renal sclerosis (Jaccoud); gouty kidney; contracted kidney; small red kidney.

Presence of Albumin.—"Even as the urine of parenchymatous nephritis so does that of interstitial contain albumin almost always, but while in the first affection albuminuria is the chief phenomenon and excels all the other phenomena in importance, in the latter albumin is a secondary and contingent phenomenon."

To these words of Rendu, which emphasize the difference in the symptom albuminuria in these two varieties of Bright's, we must add (and this diminishes considerably the value of this symptom in case of the small red kidney) that albuminuria in interstitial nephritis presents marked variations both as regards quantity and progress.

The amount of albumin is ordinarily feeble; it occurs as a slight opalescent cloud, rarely flocculent, appearing slowly and at the end of a few seconds. "This slight proportion of albumin is characteristic of interstitial nephritis, for it is one of the most constant modifications in the urine."[46] A superficial examination may readily not determine it; the urine must hence be examined with great care, and the slightest cloudiness should excite the suspicion of the physician.

According to Wagner[47] the urine of interstitial nephritis does not contain more albumin to the 1000 than that of parenchymatous nephritis does to the 100. The amount that transudes through the renal filter does not usually exceed a few centigrammes, rarely reaching 2 grammes in the twenty-four hours. Bartels[48] gives the following figures: 1 gr. 03, 1 gr. 48, 2 gr. 16. Exceptionally it surpasses these figures, and then at the end of the disease.

Even as in parenchymatous nephritis the albumin varies according to the stage of the disease; it varies frequently enough from day to day.

It is not in the first stage of the disease that albuminuria is established permanently; it develops by starts. From time to time the urine becomes albuminous for a greater or less time; then the albumin disappears to reappear again, and this during months, often indeed during years; it is only at the end of a number of years of this irregular progress that it becomes permanently established.

All writers are here in accord, and the fact has been known for long. Todd [49] first noted it: he had found that frequently albuminuria followed on attacks of gout, and that it totally disappeared in the intervals. Johnson [50] confirmed in full the assertions of Todd. Bartels,[51] Lecorché,[52] Lancereaux,[53] Labadie-Lagrave,[54] Senator,[55] are all unanimous on this point. We may, therefore, conclude with Rendu [56]: "It appears, then, probable that in the first stages of the affection, albumin only appears at intervals, and that the nephritis progresses by starts."

The following case appears to us characteristic in this connection:

Case III. (*Personal.*)

Bright's Disease (*Interstitial Form*).—*Initial Stage.*—D——, æt. sixty-eight, tailor, entered hospital June 27, 1887. Antecedents good, with the exception of a typhoid fever. For the past three to four months has had the following symptoms: cephalalgia; epistaxis (morning), slight visual and auditory troubles, first phalanx of right hand deadened, nocturnal cramps, electrical starts, frequent nocturnal desire to micturate without polyuria, edema of lower extremities and of thorax.

The urine examined 29th of June to 7th of August, presented the following characteristics:

Slightly acid or neutral; sp. gr. varying between 1.009 and 1.015, the quantity varied between 1.250 c.c. and 2500 c.c., the mean amount being 1675 c.c.

Albumin appeared and disappeared for varying intervals. From 29th June to 3d July inclusive the amount of albumin varied from .35 gr. to .55 gr. From July 4th to July 12th complete absence of albumin. It reappeared on the 13th and persisted to 21st (.35 gr. to .40 gr.). It disappeared July 21 to August 7, and then the patient passed from under our notice.

Absolute milk diet bettered his condition markedly.

English writers are much more affirmative; some of them contend that renal sclerosis, in its first stage, is not accompanied by albumin, and they have called this stage the pre-albuminuric; this opinion, first expressed by Milner Fothergill,[57] has lately been accepted by Mohamed in a number of papers.[58]

Although we cannot admit the pre-albuminuric stage of the English writers, we coincide fully with the French opinion, which seems to us well established: at the beginning of interstitial nephritis albumin appears in the urine after a transient fashion, and this intermittency seems to us the true characteristic of this first period. At the end of a number of months, or of years, when the sclerotic lesions have progressed, the intermittent albuminuria becomes permanent, although it is still subject to variations of which we will speak.

"The quantity of albumin passed in interstitial nephritis may be so great as not to differ at all from that met with in the course of primitive parenchymatous nephritis."[59] Usually, however, it is not pronounced until the latter stages of the disease.

At this period the amount diminishes according to some: "In all cases albumin diminishes towards the end of the disease."[60]

"It diminishes again, and even completely disappears when the vital forces are lowered and the heart weakens."[61]

According to other writers it increases: "In the last stage of life it is not rare to find very abundant flocculi of albumin even as in parenchymatous nephritis; it would then be very difficult to make a differential diagnosis if we did not know the previous march of the disease."[62]

"In a number of analyses made at an advanced stage of the disease I have seen it vary from 10 to 15 grammes.[63]

The albumin, further, is subject in quantity to daily variations.

Gubler,[64] in a paper read before the *Société de biologie* the 6th of August, 1853, describes, in general, these variations in amount, dividing them into periodic, accidental and diurnal variations; he dwelt in particular on the latter. According to him albumin is ordinarily present in greater amount during the daytime; the contrary holds, however, for those who work at night. Bartels[65] has confirmed these views, and has shown

the marked oscillations occurring in the same individual in the course of interstitial nephritis, oscillations, further, in accord with his manner of living, food, and general state of nutrition.

In a number of instances he has noted the alternate disappearance and reappearance of albumin; in one case he checked this for seven months. During this whole period albumin was found in the day urine and no trace in that of the night; when the patient passed his days in bed the albumin disappeared from the urine to reappear when he left his bed for the day.

Wagner[66] has noticed the same fact as Bartels; in certain cases albumin is absent from the night urine, while that of the day, especially when the patient was active, contained a certain amount. Ellis[67] has also noted that the absence of albumin often coincided with rest in bed.

Patients weakened by privation usually have little albumin in the urine when they enter the hospital; as their nutrition increases, the albumin often increases.[68]

Absence of Albumin.—Although it is an established fact that albumin may be absent for a greater or less time in case of renal sclerosis, especially in its early stage, a less established fact, and one less acceptable to pathologists, is the possibility of the non-appearance of albumin during the entire course of the disease.

"The urine, in case of granular kidney, may or may not be albuminous," so wrote Wilkes (1852) in Guy's Hospital Reports.

Since, this question has been discussed by many writers; all have answered it identically, as prove the following quotations; some admit with Bartels that every nephritis must at some time be accompanied by albuminous urine:

"Albuminuria is not a constant phenomenon, as recent observations have proved for me. Füngel mentions that absence of albumin in the urine of his patients has often led him into the error of not recognizing the disease. But neither Füngel's observations nor mine, nor those of others, prove that albumin may be lacking during the entire course of the disease. Albuminuria is, in any event, one of the most characteristic symptoms."

A few pages further on, Bartels[69] cites the only case which he has seen of renal atrophy, verified by autopsy, which, during life, was never accompanied by albuminous urine; and there-

fore, he adds, the existence of the renal disease was not determined.

Many writers, still, are of the contrary opinion; they claim that albumin may be absent in renal sclerosis.

"The urine need not contain albumin; the disease may run its course without there being present the slightest trace; this is when interstitial nephritis has remained uncomplicated by canalicular trouble; usually, however, albumin is present."

Mahomed [70] and Millard [71] are still more positive; according to them interstitial nephritis is not usually accompanied by albuminuria; albumin only appears when epithelial alterations occur.

Between the view of Lecorché and that of Mahomed and Millard there is an intermediate view, that of Professor Dieulafoy.[72] He has proved that there exists Bright's disease without albuminuria, and this he has described in his two papers last year at the Academy of Medicine, and this year in his lectures at the school. We agree perfectly with this view and have often proved the truth of it.

We cite a few cases which prove this point. We give first, in abstract, two cases cited by Dieulafoy in his papers read before the Academy, of peculiar interest in that the diagnosis was confirmed post-mortem.

Case IV. (*Dieulafoy.*)

Bright's Disease (*Interstitial Form*).—*Absence of Albuminuria.*—*Autopsy.*—A woman æt. forty-seven was admitted to the hospital March 19, 1886. Her symptoms were angina pectoris, cephalalgia, frequent desire to micturate and marked sensation of dead finger.

Fifteen days before admission she had a violent attack of angina and there followed edema of the feet and of the legs (March 15). She had, on auscultation, pulmonary edema of the right base; the urine was scanty, high-colored, no albumin. M. Dieulafoy diagnosticated Bright's disease of two years' duration.

March 20, 400 c.c. urine, no albumin.
March 21, 700 c.c.; no albumin.
March 22, 1.500 c.c.; no albumin.
March 23, 2.600 c.c.; no albumin.

The increase in the amount of urine coincided with betterment in general condition as the result of diuretics and milk diet.

The patient caught cold on the 24th; generalized bronchitis

set in and she died on the 25th. The amount of urine fell to 258 gr.; trace of albumin.

At the autopsy the kidneys were of the normal size, and each contained three to four cysts. Histologically, evidence of interstitial nephritis with arterio-sclerosis predominating.

This conclusive case proves clearly that interstitial nephritis may progress without albuminuria; the slight trace of albumin found on the last day does not invalidate this conclusion.

CASE V. (*Dieulafoy.*)

Interstitial Nephritis.—Absence of Albumin.—Autopsy.—This case concerns a patient with Bright's complaining for a considerable time of violent cephalalgia (like that of syphilis), of attacks of oppression, of cramps, absence of sensation in finger, increased desire to micturate, the urine being of mean amount and containing no albumin (6th to 12th of July).

On July 12, bronchitis developed; the urine decreased to a litre, and albumin appeared to the amount of .95 gr. daily up to death.

At autopsy: nephritis with arterio-sclerosis.

We might cite many other cases which we have seen, although, unlike the preceding, we have not the evidence yielded by autopsy. The question seems to us adjudicated in the affirmative. Side by side with the large class of cases of Bright's disease with albuminuria must be ranked the increasing class of Bright's without albuminuria.

We may resume, then, as follows:

The presence of albumin in interstitial nephritis is subject to great variations; ordinarily intermittent at the outset, it usually shows itself when renal sclerosis has progressed.

The absence of albumin during a greater or less period, at the beginning and end of the affection, is frequently noted; it is likely that such may be the case during its entire course. Although we think the English and American views too absolute, we do not question but that there exist cases of Bright's without albuminuria. These cases are few in number to-day, but they will become more frequent. With a deeper knowledge of the many symptoms of Bright's the disease will be better recognized and this too without waiting for the appearance of albumin in the urine—the too common tendency of to-day.

Mixed Diffuse Nephritis.—Between these two extreme types of chronic nephritis, the one of which is characterized by

the large white kidney with exclusively epithelial alterations, and the other by the small granular kidney with interstitial proliferations, there occurs a mixed type, where sclerosis is mixed with epithelial degeneration, where the inflammation is diffused through all of the renal parenchyma. It is difficult to trace the clinical history of this form, since both the lesions and the symptoms are varied and complex.

Although from the preceding considerations we have been able to clearly prove that albumin is abundant and almost constant in parenchymatous nephritis, and that, on the other hand, it is in small amount and irregular in appearance in interstitial nephritis, it is very difficult to draw the slightest conclusion in this respect in the numerous varieties of mixed nephritis. We might try to classify these nephritides in different secondary groups, basing them on the progress of the affection and on the symptoms peculiar to them; but this division seems to us too schematic, and consequently little in accord with clinical data. Therefore, without emphasizing the diverse combinations which may be met with and the different cases of chronic diffuse inflammation of the kidneys, we will content ourselves with the statement that a close examination readily allows us to say whether the case approximates a parenchymatous or an interstitial nephritis. Having established this point, we may deduce the progress and the characteristics of albuminuria in a given case:

The more the parenchymatous lesions are marked, the more abundant will be the albumin and the more constant its appearance.

The more the interstitial lesions predominate, the less will be the albumin and the more irregular its presence.

According to Wagner,[73] who has been able to follow for a long time a large number of cases in his private practice, diffuse nephritis, which is by far the most common form, and which he thence calls the usual Bright's disease, habitually pursues the following course:

At the outset the albumin is abundant and permanent; then, as the affection progresses, the albumin diminishes, but increases transiently from the slightest cause. Finally, when the terminal stage is reached, and this usually requires two to three years, the albumin not uncommonly disappears.

We give in abstract the following typical case:

Case VI. (*Dieulafoy.*)

Bright's Disease (Diffuse Form).—Absence of Albumin. —Death.—Autopsy.—Woman æt. twenty-nine, entered hospital November 11, 1885. In July, 1884, the symptoms were vomiting and hematemesis; in November the vomiting increased and a second hematemesis. Milk diet kept her well up to May, 1885. The vomiting then returned, accompanied by gastric and lumbar pains and by cephalalgia. In this condition she entered hospital. These symptoms together with the absence of albumin led to diagnosis of gastric ulcer, and she was placed on exclusive milk diet.

Up to December 29th the symptoms persisted; two or three times hematemesis; no albumin. Coma and death on December 29. Autopsy: stomach healthy; kidneys whitish, large, and microscopically evidence of mixed nephritis.

Here then we have a patient who was under observation for seven weeks and never showed the slightest trace of albumin, although she had a mixed nephritis.

We give a second case of Dieulafoy's, which proves conclusively that diffuse nephritis may run its course and albumin may entirely disappear for a longer or shorter time.

Case VII. (*Abstract.*)

Diffuse Bright's.—Disappearance of Albumin for 2½ months.—Autopsy.—This patient, *non compos*, had a trace of albumin on the 14th February, and on the eve of her death, May 4; in the interval no albumin whatever.

The symptoms were uncontrollable vomiting, polyuria, cramps, cephalalgia; edema and albuminuria were alone wanting. Autopsy: diffuse nephritis.

These two cases, with autopsy, confirm the views of Wagner; they suffice amply to establish the point at issue.

Nature of Albuminuria.

For long the existence of albuminuria has been known, and it was further recognized that it existed in many and in varied diseases, and then the question arose as to whether it was possible, at least readily, to distinguish at the bedside cases where the kidney was seriously diseased from those where the presence of albumin in the urine was not dependent on an alteration of the organ. With this end in view the attempt

was made to utilize the properties of the albuminoid substance determined; at the outset its action under various reagents was found out, and next the determination of its nature was aimed at.

To expose the physical characters of the albuminous coagulum, on the one hand, and its chemical characters, on the other, such is the double study we are about entering upon in order to determine the nature of the albuminuria of Bright's disease.

Physical Characteristics of the Albuminous Coagulum.— It is we believe in a brief note to his treatise on the diseases of the kidneys, that Rayer first noted the fact of the retractility of albumin, without, however, attaching the least importance to this property, as is proved by the following extract:

"After having precipitated the albumin in the urine by nitric acid, if an excess of acid be added, in less proportion than the urine, however, the albuminous flocculi almost always become crisp." [74]

Ten years later (1850) this question was studied from a clinical standpoint. In his inaugural thesis Dr. Oppenheimer Seligman [75] writes (a fact already established, however) that there exist two kinds of albuminuria:

The one transient, met with in many diseases;

The other permanent, met with in the granular affection of the kidneys known as Bright's disease.

He adds that in both cases the urine has special characteristics, and that the precipitated albumin behaves in different ways.

In case of transient albuminuria, the urine is high-colored; it has never the lactescent whiteness of the urine of Bright's; the albumin, under the influence of reagents, precipitates with difficulty in flocculi.

In case of permanent albuminuria, connected with Bright's disease, the urine is lactescent, opaline, and almost always whitish; when subjected to reagents the albumin falls quickly in condensed flocculi, snow white or at least clear opaline.

This question of the physical characteristics of the albuminous coagula has been studied again, a few years later, by Professor Bouchard (November, 1880).

In a paper read before the Congress at London on the in-

fectious nephritides, and in two papers read before the Clinical Society, he establishes the following facts which result from the study of many cases of albuminuria.

When coagulated albumin is subjected to the action of heat, it happens that at times the coagulum retracts into flocculi and leaves the urine perfectly clear. On the other hand, a simple homogeneous, lactescent cloud is produced. These two albumin states correspond to two pathogenetic conditions altogether different.

The retractile albumin is that of normal, intact blood, which is able to pass on account of an alteration in the renal filter; this is the albumin which is met with in diseases of the urinary tract, and especially in nephritis.

The non-retractile albumin is an abnormal albumin, capable of dialysis, notwithstanding the integrity of the renal filter; it is found in diseases accompanied by high fever (typhoid, erysipelas, pneumonia, pleurisy, etc.).

This differential property was most important; but, unfortunately, other researches soon invalidated it. Soon after its birth the theory of Bouchard was actively attacked.

Cazeneuve and Lépine, in two papers read before the *Societé Biologique* (November, 1880), showed that retractility or absence of retractility depended not on the intimate nature of albumin, but on the chemical composition of the medium in which the coagulation was affected. If the urine were acid enough the precipitate forms in flocculi; if, on the other hand, it is too acid or not enough so, the urine is clouded, and this changes into flocculi when, according to the case, the liquid is neutralized or sufficiently acidified. Rodet [76] corroborated these views.

The chemical composition, then, of the medium in which the coagulation takes place has a manifest influence on the constitution of the precipitate. Other conditions, which must be taken into account, also have an influence; on the one hand, the quantity of albumin present, and, on the other, the degree of concentration of the urine. These views of Bouchard have been fully confirmed by our colleague, Capitan,[77] in his inaugural thesis; we quote the following passage, which clearly states the case.

"If we examine a normal urine, to which has been added a determined quantity of egg albumin, or a diluted urine of

which we know the amount of albumin present, we will see that proportionately as the quantity of albumin decreases we obtain successively large, medium and small flocculi, and finally the cloud of non-retractile albumin. This in turn ceases to be perceptible."

Let us, for instance, subject to the aceto-picric reagent and to heat different solutions more or less rich in albumin: We note the following facts:

In a sol. 1 gr. to 1000, abundant flocculi of mean size. In a sol. 50 gr. to 1000, abundant, but small flocculi. In a sol. 25 gr. to 1000, very fine, sand-like flocculi. In a sol. 12 to 1000, uniform slight cloud. In a sol. .06 to 1000, doubtful cloudiness. In a sol. .03 to 1000, nothing apparent.

In his different experiments Capitan used different reagents and always determined the following fact:

In proportion as the albumin in a given liquid diminishes, so does the precipitate become less marked; it even ends by disappearing if the amount of albumin is very slight.

These physico-chemical conditions of the albuminous medium invalidate almost completely the clinical value of the manner in which the albumin coagulates. We do not claim, however, like certain writers (Brucke), that the appearance of the coagulum is the worst of all the characters which assist in distinguishing the different varieties of albumin, for in certain cases this appearance may be of great value.

Although, as has clearly proved Professor Jaccoud,[78] the retractile albumin may be met with in typhoid fever, in simple angina, and in pneumonia without there being marked change in the kidney, one fact is certain, and this is that every marked case of nephritis is accompanied by retractile albumin; therefore we may, with great probability of being right, whenever, by whatever method, we obtain a rapid and abundant retractile precipitate, admit the existence of a renal lesion.

May we go further? May we thence deduce the age of the lesion? Jaccoud thinks this possible;[79] witness the following passage which we take from one of his lectures on parenchymatous nephritis:

"I can affirm that the following characteristics only belong to an old nephritis; large flocculi form at once, and they are of a dirty-green color."

We simply cite this fact. It has not been noted by other writers.

Chemical Characteristics of the Albuminous Coagulum.—If the physical characteristics of the obtained albumin have only a limited diagnostic value, does the same hold for the chemical? We must now try to answer this question.

Although thirty years have passed since the discovery of different kinds of albumin in the urine, we are not at one as yet in regard to the value of each species, although some are thoroughly known.

Studied, at the outset, by Mialhe from a purely chemical stand-point, next referred to by certain writers as curiosities, for a long while they were deemed without value. It was only later that the attempt was made to attribute to these different kinds of albumin a significance which we are going to try to expose in stating the question of urinary albumins from the actual stand-point of to-day.

As we have seen, we may find four varieties of albumin in the urine: serin, globulin, peptones, and hemialbuminose or propeptone. We have already exposed their peculiar characteristics, and have already stated the methods of differentiation; we must now determine their clinical value.

Serin.—The albumin of serum or serin is the most important, beyond question, of the urinary albumins; it is, to borrow Jaccoud's happy expression, the albumin of Bright's, *par excellence*. Abundant and constant in parenchymatous nephritis, rare and intermittent in interstitial nephritis, it exists in all cases of Bright's disease, at least in those which are accompanied by albuminuria. The same remarks hold true for serin as did for this symptom, and we need not dwell on it further.

We are content then with simply mentioning serin, and we pass at once to the clinical history, far less known, of the other urinary albumins, globulin, peptones, and propeptones.

Globulin.—Lehmann,[80] one of the first to call attention to this albuminoid substance, found it in nephritic urine; according to him it is present with serin, although in less proportion. Edfelser[81] grants the view of Lehmann, but established the fact that the quantity of globulin was in direct proportion to that of serin. Such is not, however, the opinion of Gerhardt,[82] who, while admitting the existence of globulin, claims that it is not found in the urine of all cases of Bright's. Fuhry-Suethlage[83] and Leube[84] have also detected it, the first in a case of diffuse nephritis, the second in a case of parenchymatous nephritis.

Petri[85] has made numerous analyses; in fourteen cases of chronic nephritis he only found globulin four times. It is in particular Senator,[86] of whose competence in regard to albuminuria every one testifies, who especially studied this question (1874-1878). Not satisfied with finding globulin in albuminous urines, he queried if we might judge the character of the renal affection by the greater or less quantity of globulin. With this end in view he determined the quantity of this substance present in the different forms of nephritis; he found that it was particularly abundant in case of the amyloid kidney, and in acute nephritis; he also found it in chronic nephritis; rarely in diffuse nephritis; directly in proportion to the amount of serin in circumscribed nephritis; therefore Senator concluded that in chronic nephritis the amount of globulin met with has a true diagnostic value, for it allows us readily enough to differentiate the different varieties.

The views of Senator are far from being accepted without protest; not alone in Germany, but also in England and in France, this question is far from being accepted.

In Germany, Heynsius[87] claims that the presence of globulin furnishes absolutely no information in regard to the nature of the disease.

Hoffmann[88] established by numerous analyses that the connection existing between the amount of globulin and of serin may change notably in the same patient; consequently a diagnosis based on the relations existing between these two albuminoid substances may lead to marked error.

In England, Laundby[89] is not less affirmative; in an important work which appeared in 1880, he concludes that globulin exists rarely enough in the urine, and always concomitantly with serum albumin; consequently it cannot as yet answer as a characteristic of a morbid group.

The same views are current in France; it suffices to quote the following passages which we borrow from two clinicians who have especially studied the subject of albuminuria:

"The valuation of globulin in the urine furnishes no presumption in regard to the nature of the renal affection."[90]

"It is impossible to establish any connection between the nature of the renal lesion and the presence of globulin in albuminous urine. In consequence globulin proves nothing in regard to the existence of a renal lesion; if this lesion is not

made probable by other symptoms it tells us nothing either as to the nature or the degree of the lesion; it possesses then no diagnostic value whatever in regard to the state of the kidneys; it is purely an index of a non-determined modification of the condition of the blood."[91]

A few pages further on Jaccoud, after having insisted on the importance clinically of separating these two urinary albumins, claims that globulin exists in false albuminuria, and in the transient albuminuria which occurs during the progress of or as a sequel to acute diseases, and which depends on the modification of the proteid substances of the blood by the acute disease. In this connection he refers to a patient with acute pneumonia; the urine subjected to the ordinary reagents gave a precipitate; deprived, according to rule, of globulin by the sulphate of magnesium, it gave no further precipitate by any reagent; in this case of pneumonia the urine was totally lacking in serin and contained only globulin.

This fact is very interesting; we need other similar cases in order to accept the ingenious opinion of Jaccoud. Quite recently certain papers have appeared on this subject.

The most complete and most conscientious is without question that of Dr. Kamensky,[92] published at St. Petersburg in 1885. After an analysis of the question, he states the results of his researches: he determines with great care the daily amounts of globulin and of serin; he next establishes the difference between them; he next compares the relation existing between the total amount of albumin and the serin. Of the four observations of this writer one alone allows of conclusions, and we give it in abstract.

Case VIII. (*Kamensky.*)

Chronic Diffuse Nephritis.—B.——, baker, æt. 31, alcoholic and syphilitic. In the spring of 1884, symptoms first appeared. Swelling of the face in the morning, edema of the legs at night, occasionally violent cephalalgia.

Patient entered hospital 19th September, 1884; abundant flocculi of albumin in the urine.

The first exact analysis was made the 27th of December, the last the 18th March, 1885. Here are the figures:

Date.	Quantity of Urine.	Percentage.	Total Weight Albumin.	Weight of Serin.	Weight of Globulin.	Relation to Amt. of Albumin.
Dec. 27, 1884.	1,700 gr.	.77	13.22 gr.	9.65 gr.	3.57 gr.	2.70
Jan. 9, 1885.	2,500 "	1.02	24.60 "	14.86 "	9.80 "	1.61
" 19, "	2,730 "	.96	26.24 "	18.85 "	7.39 "	2.55
Feb. 25, "	1,830 "	1.17	21.48 "	14.24 "	7.24 "	1.95
" 28, "	2,400 "	.63	15.34 "	10.60 "	4.74 "	2.33
Mar. 1, "	2,800 "	.42	11.83 "	8.90 "	2.93 "	3.44
" 18, "	2,200 "	.57	12.53 "	9.44 "	3.12 "	3.02

If we examine this table we may determine, generally, the following facts:

We cannot establish any comparison between the amount of albumin and fractions of albumin.

We may deduce the fact that the relation of the albumin is not constant; generally, it diminishes as the serin increases, and it increases as the latter diminishes.

An examination of the three other observations does not allow the same deduction. Therefore Kamensky concludes that in a given case there does not exist any relation between the amount of albumin and that of globulin, and that the latter, hence, has little diagnostic value.

As for us we regret that in this interesting study the writer did not take into account the relation existing between the amount of albumin and the general state; and he might possibly have drawn some striking conclusions. This point he has not at all considered, nor have any other writers on the subject.

After Kamensky's work it remains for us to notice that of Chéron,[93] which appeared last year in *l'Union médicale;* in his review of the clinical value of the varieties of urinary albumin our colleague accepts entirely the ideas of Jaccoud. He insists on the importance of differentiating these two urinary albumins, which are precipitated by the same regents, because:

"Globulin does not indicate a renal lesion when it exists alone.

"When it coexists with serin the amount of the latter is alone important in diagnosis."

In the experiments we had occasion to make for a greater or less time on twelve patients, we found globulin only in four; this urinary albumin, usually in small amount, was found on different occasions for two or three days; it appeared and disappeared without our being able to note anything special in the condition of our patients. We must mention, however, that in the last patient in whom we found it, the appearance of the globulin and its increase have coincided with the appearance of a violent uremic headache, the prelude of sharp attacks of eclampsia, in the midst of which our patient died.

We here report the four observations of globulinuria which we have met with:

Case IX. (*Personal.*)

F——, æt. twenty-four, entered the service of Professor Dieulafoy, Hospital Necker, June 21, 1887.

This woman, at the time of her first pregnancy (two and a half years previously), had urinary disturbances, among others frequent desire to micturate. A few months after delivery, she complained of sharp pains in the right lumbar region, soon followed by persistent oppression and cough. A physician from the *Hôtel-Dieu,* who then saw her (March, 1885), diagnosticated bronchitis and placed her on milk diet, under which *régime* she improved rapidly.

One month later the same symptoms appeared and in addition swelling of the eyelids and marked edema of the legs; she again went to the *Hôtel-Dieu* and was again placed on milk diet.

She improved, but two months later the symptoms became aggravated and she was admitted to the *Hôtel-Dieu.* Absolute milk diet again caused disappearance of symptoms.

From August 2, 1885, to November 15, 1886, the patient remained well, symptoms being held in check by occasional milk diet.

From November 15, 1886, her health deteriorated; nausea and at times uncontrollable vomiting was added to the dyspnea and the edema; next there followed nocturnal cramps, recurring about every eight days, epistaxis, slight, in the morning, urinary disturbances. All other symptoms of Bright's were lacking.

In this condition the woman entered the hospital. Under milk diet she rapidly improved, and on the 3d of July she seemed in perfect health.

The examination of the urine made daily from the 22d of June to the 15th of July showed:

The urine, usually slightly acid, had a specific gravity of 1008 to 1010.

The quantity varied from 3000 c.c. to 1500 c.c.; the mean quantity being 2290 c.c.

The amount of albumin varied from 9.25 gr. (July 6th) to 0 gr. (July 15th) the mean daily quantity being 6.30 gr.

At various times we noted the presence of globulin:

June 22d, 2.50 gr.; 24th, 25th, 28th, 30th of June and the 1st of July, only traces.

On the 10th of July it appeared as a flocculent cloud floating in the liquid; she then had headache and slight visual disturbances. The globulin persisted to the same degree the 11th to the 14th inclusive, the cephalalgia disappeared on the 13th, as also the visual troubles.

On the 15th the globulin reached the amount of 2 gr. to the litre, or 4.50 gr. total quantity; the liquid cleared of the abundant precipitate yielded by the sulphate of magnesium contained no trace of albumin.

On this day F—— left the hospital. We have never seen her again, and we regret this, for the case was of great interest. Such as it is it proves that globulin, in its evolution, follows an intermittent course, and that it appears or disappears without appreciable cause.

Case X. (*Personal.*)

C——, æt. fifty-one, entered hospital May 17, 1887, service of M. Rigal. In perfect health up to the end of 1885, without known cause he was seized by shortness of breath on climbing the stairs, and by edema of the legs and eyelids. Soon thereafter appeared frequent nocturnal micturition, cramps, dumbness of phalanges of left hand.

He entered Necker and his urine was found loaded with albumin; at the end of a month he was discharged cured, without albumin.

For a year to a year and a half his health was perfect and he kept at his work. Early in May, 1887, the symptoms returned and he again entered the hospital. The legs were edematous as well as the face and the thorax; the amount of urine was normal, but it contained albumin in marked amount; no other symptoms of Bright's. He was placed on milk diet and dry cups to loins were ordered daily.

The urine examined daily from the 17th of June to July 10th showed us the following:

Urine feebly acid; specific gravity varying from 1008 to 1018.

The amount varied from 800 c.c. to 2000 c.c.; the mean amount being 1110 c.c.

The quantity of albumin varied from 1.4 gr. to 4 gr.; the mean daily quantity being 2.5 gr.

The globulin appeared, irregularly, on several occasions:

On June 10th, 19th, 20th, about .50 gr.; the 21st, 22d June only traces. On 29th and 30th June it again appeared as a slight flocculent cloud, and again on the 3d and 4th July; finally on July 6th and 8th the cloud was a trifle more marked.

During this interval there was nothing specially marked in the symptoms; from June 28th all symptoms of Bright's disappeared. Since then the patient has been in good health.

This observation is especially of interest in that it concerns a case of Bright's without albuminuria.

Case XI. (*Personal.*)

Bright's Disease.—(Interstitial Form.)—Absence of Albumin; Intermittent Globulinuria.—R——, æt. sixty, entered hospital June 17, 1887, with paresis of right lower limb, which had followed a fall from the third story in July, 1886. He complained further of shortness of breath and frequent desire to urinate. He had also edema of the legs and eyelids, cramps in the calf, epistaxis, a few drops, in the morning. He had, further, a few visual disturbances and deafness of both sides; *bruit de galop* quite marked.

Under milk diet he improved rapidly, the edema and most of the other symptoms disappearing in a few days. The shortness of breath persisted to the end of July.

The urine from the 29th of June to August 12th presented the following characters:

Slightly acid, alkaline or neutral; specific gravity varying from 1005 to 1016.

Maximum amount 4000 gr. July 6th, minimum amount 1100 June 29th; mean daily amount 2910 c.c. At no time albumin. Globulin appeared on three separate occasions, always in scant amount; on the first occasion July 2d, on the second July 6th to 17th, on the third August 3d (quite distinct cloud).

This observation of a Bright's patient without albuminuria is the only instance where we have found globulin. Dr. Estell of Lyons, in his thesis, reports two cases where globulinuria alone existed, the first concerning an atheromatous patient, the second an ataxic.

Case XII. (*Personal.*)

Bright's Disease, Diffuse Form.—Albuminuria, Globulinuria, regular in its course, Eclampsia, Death.—G——, æt. twenty-five, entered the service of Professor Dieulafoy

November 22, 1887, for edema of limbs and dyspnea. Two and a half years ago the patient caught cold and then suffered from violent cephalalgia and anasarca; the urine was scanty, not bloody, and contained flocculi of albumin; he had been placed on milk diet and followed this for three weeks. Since that time he has only complained of occasional cephalalgia and of frequent micturition without excess in amount.

From September, 1887, his cephalalgia became more frequent and intense; at times he was nauseated and had bilious vomiting; often edema of the legs; sometimes a little swelling of the eyelids in the morning. He caught cold November 14, 1887; suffered from slight fever, cough and hoarseness.

On entrance into hospital he had laryngo-tracheitis and slight bronchitis, frequent, distressing cough, abundant gurgling, sub-crepitant râles scattered over the lateral thorax. On examining the urine we found flocculi of albumin and he was placed on milk diet.

November 24, urine slightly acid, 2400 c.c., 6 gr. albumin (only serin).

November 25, urine acid, 2300 c.c., 5¾ gr. albumin.

November 26, urine acid, 2350 c.c., 5 c.c., 20 albumin.

November 27, slightly acid, 2300 c.c. 4¼ gr. albumin.

The laryngo-tracheitis has gone and patient feels well.

November 28, urine acid, 2200 c.c., albumin 5.20 gr.

November 29, slightly acid, 1800 c.c., 2¼ gr. albumin.

November 30, 1600 c.c., slightly acid, 2.40 gr. albumin, slight cephalalgia.

December 1, increase of the cephalalgia; urine very alkaline, lactescent, charged with urates, 1500 c.c.; 2¼ gr. albumin; first appearance of globulin (sulphate of magnesium test).

December 2, headache persists; urine slightly acid, clearer, 1500 c.c., 2.60 gr. albumin, globulin manifest.

December 3, more headache, insomnia, urine 1300 c.c., 2.60 gr. albumin; flocculi of globulin.

Treatment: 1 leech to nucha; sinapisms.

December 4, continuous headache; insomnia, nausea; urine alkaline, 1300 c.c., 1.65 gr. albumin, globulin.

December 5 symptoms worse; urine still alkaline, 1600 c.c., 1 gr. serin, .60 gr. globulin. No urine during the day, the bladder empty, by catheter.

December 6, at 5 o'clock A.M., first attack of eclampsia. 6 leeches behind the ears.

At 5¾, second attack; at 6¾, third; at 8, fourth; at 9, fifth; at 9¾, sixth; temperature 37.3°, venesection to extent of 800 gr.; inhalations of oxygen.

At 10½, seventh attack; at 11½, eighth. At noon, return of consciousness, and desire for sleep.

At 10½, evening, ninth attack; death.

Autopsy 36 hours P.M.: lesions of diffuse nephritis.

Before we can give a personal opinion we need more cases; for the time being we are obliged to rest content with the narration of our observations. We have only proved that globulin does not exist in all cases of chronic nephritis; when it does exist it seems to follow a rather irregular march, appearing and disappearing without appreciable cause.

Peptones.—We have not determined as much in regard to peptones. On many occasions we have hunted for them in our albuminuric cases, both by the direct method which seems to us quite imperfect, and also by precipitation by the acetic solution of phosphotungstate of soda; we have never found them. We have also often examined from this stand-point the urine of cases of Bright's without albuminuria, and we have never obtained the reaction of peptones.

Are our methods of research imperfect? We have always used the methods which are recommended. Must we admit that peptones are rarely found in albuminous urine? This we cannot answer.

This question of peptones is indeed much in dispute; according to some, albuminuria and peptonuria are often associated, and according to others they are never.

We are here naturally led to sketch briefly the history of our third species of urinary albuminuria.

Described by Mialhe[94] under the name of albmuinuria, studied by Gerhardt[95] under the name of latent albuminuria, the peptones were especially studied from a clinical stand-point in Germany and in Italy.

In Germany peptones have been found in the urine of Bright's by a number of observers, Eichwald,[96] Obermuller[97] and especially Senator,[98] who has detected them in all febrile and afebrile conditions characterized by the presence of coagulable albumin in the urine; Pétri[99] found them nine times in fourteen of chronic nephritis. Maixner[100] and especially von Jacksch[101] have thoroughly studied this question; the latter studied 354 cases, which include 762 urinary analyses, but we do not find mention of renal affections.

In Italy writers are not so affirmative in regard to the association of albuminuria and of peptonuria. Pietro Grocco[102] of Paris considers peptonuria as utterly independent of albuminuria; it is found especially in case of local inflammatory and suppurative processes, rarely in chronic affections.

This interesting question of peptonuria has been studied in France from a different stand-point; its connection in renal disease has attracted little attention.

"Peptonuria may appear indifferently in all cases of Bright's; it presents nothing in accord either with the nature of the lesion nor with the existence of a lesion; it depends on the state of the blood and not on that of the kidneys." [103]

It seems then that if peptones exist in albuminuria their presence has no diagnostic import.

8. *Hemialbuminose.*—This little known agent has been found in renal affections; Fuhrbinger and von Jacksch have found it, the former twice, the latter once, without drawing any deduction. Lépine thinks that its presence points to a dyscrasia worth nothing.

Connection between Albuminuria and the Urinary Secretion.

Now that we know the information which the existence and the nature of albuminoid substances in the urine may give us, we must seek if there do not exist relations between albuminuria and the urinary secretion, and if it be not possible to draw from such relations certain considerations useful from the diagnostic point of view of Bright's disease.

We will consider as before parenchymatous nephritis, interstitial nephritis, and diffuse nephritis; the two former in particular since their characteristics are more marked, although the diffuse form is the most frequent. We must pass successively in review the physical characters, the chemical characters, and the microscopic characters of the urinary secretion in chronic nephritis.

Physical Characters of the Urine of Bright's.—Although in the majority of cases the urine of Bright's presents certain external characteristics which at first sight differentiate it from normal urine, we must bear in mind the fact that these characters are of secondary importance and are not of much assistance in establishing a diagnosis.

Although it is true that the urine is yellow, deep, more or less cloudy in parenchymatous nephritis, and pale, transparent, opalescent in interstitial nephritis, there are many modifications to these statements. Further, we must not forget

that, at the outset, the urine of chronic nephritis is like normal urine.

The same remarks hold true for the reaction and the specific gravity. In short, there exists, among the external characteristics of the urine, only one which we think is of importance: this is the quantity of urine passed, and on this point we will dwell somewhat. We wish first to insist upon the fact that all the urine passed each day must be measured.

Parenchymatous Nephritis.—Although we do not know much about the quantitative modifications which occur in the first stages of the large white kidney, we know that at this time the amount of urine secreted is usually below the normal; all writers are here in accord except Frerichs,[104] who contends that at this period the amount is increased; probably this observer, as have pointed out Lecorché and Rendu, has confounded primitive parenchymatous nephritis with certain forms where the lesions of the large white kidney are associated with lesions of renal sclerosis.

The urine rarely exceeds 1300 to 1500 grammes; it generally oscillates between 900 and 1000 gr. (Rendu), 500 to 600 gr. (Charcot), 350 to 800 gr. (Lécorche), 698 gr. (Bartels)—such is the mean amount he has deduced from 122 observations; at any rate the amount remains much below the normal, as long as the inflammation is of the same degree of intensity (Bartels).

An important point is that the amount varies greatly from day to day; the amount of drink taken, the method of treatment, the period of the disease, the intercurrent affections, these are factors which modify more or less the amount of urine passed; it appears difficult then to lay down any hard and fast rule (Rendu).

In advanced stages of the disease the amount may attain the proportions indicated by Frerichs. This increase is also noted when the nephritis tends towards cure. "As soon as the nephritis runs a favorable course the quantity of urine increases." (Bartels.)

Interstitial Nephritis.—From the start, the quantity of urine is increased; polyuria exists, particularly at night, and this fact attracts the attention of the patients, so that we are able to determine quite readily the beginning of the disease. This polyuria varies, however, with the patient. In some the amount does not exceed 2 litres; in others it attains 3 to 4 litres and even 5 to 6 litres (Bartels).

The polyuria, further, is not constant in its progress, often indeed we see it replaced by a true dysuria. One fact is established, and this is that in the later stages of renal sclerosis, when the heart begins to fail, whatever the cause, the amount of urine diminishes notably, in some instances as low as 180 to 200 gr. daily; in other cases a short time before death there occurs complete anuria, usually followed by uremic accidents; after the cessation of these accidents it is not unusual to see the amount of urine increase.[105]

Diffuse Nephritis.—In the numerous intermediate varieties, where the parenchymatous lesions are mingled with the interstitial, the course of the urinary secretion is very variable. According to Wagner the urine is at the outset diminished in amount; little by little, as the color of the urine becomes paler, the amount increases until at the end of a few months it passes the normal. Still, from time to time, under the influence of various causes (catching cold, for instance), the amount diminishes coincidently with an inflammatory or a congestive attack. These changes in the amount of urine in diffuse nephritis progress besides with the albuminuria; scanty when the albumin is abundant, the amount of urine increases as the albumin diminishes. It is not always so, however; in our eleventh case, which appears to be one of diffuse nephritis, we note the figure for the urinary secretion and that for the albumin diminish concomitantly.

Such are the various external characteristics of the urine in Bright's disease, can we draw any deductions from the side of diagnosis?

Professor Lépine, of Lyons, at the Congress of the *Association française pour l'avancement des Sciences*, held at Grenoble in August, 1885, laid down certain fixed rules in regard to the value of the symptom albuminuria; he tried to prove that, although in many cases a persistent albuminuria is a symptom of ill-omen, it is yet insufficient alone to allow us to affirm the existence of a serious lesion of the kidney; in other cases, however, in connection with many other symptoms it becomes a valuable sign of Bright's disease. According to the Lyons professor here are certain of the conditions:

Albuminuria, he says, is a positive sign of chronic nephritis, in case it appears in one of the following conditions:

In large amount:

The percentage increasing concomitantly with the polyuria:

Medium percentage, but total quantity exceeding 8 gr. (owing to the coexisting polyuria):

Small percentage, but persisting for a long time.

A few months afterwards one of his pupils, in his inaugural thesis, endeavored to prove the correctness of these observations. Manin, indeed, reported some conclusive facts in his article "*De l'albuminurie comme signe du mal de Bright.*" It seems to follow clearly from this study that when albuminuria is present under certain conditions specified by the professor at Lyon it may be considered as a true index of the disease.

Of these four conditions the first and the third are frequently enough met with; the two others more rarely, but they are still important, particularly the second; this characteristic, indeed, according to Lépine, allows us to differentiate Bright's albuminuria from cardiac where the percentage of albumin diminishes as the quantity increases. Too frequently, however, these two forms of albuminuria are present together, and this is apt to invalidate our research.

For our part, we have as yet been unable to verify all the assertions of the Lyons school; but we are inclined to admit the first and the fourth conditions, which are often clinically true.

Chemical Characteristics of the Urine of Bright's.—Do the chemical properties of the urine of chronic Bright's give us analogous information? In certain cases may they give us true indices of the affection? These points we proceed to study.

The modifications in the chemical composition of the urine of Bright's have for long excited attention; since it was established that albuminous urine was not the exclusive property of renal affections, and that it was found in numerous affections, local and general, the attempt was made to find out if the albumin of Bright's did not accord with certain peculiar changes in the composition of the urine. English physicians, in particular Christison and Gregory, declared that albuminous urine had a low specific gravity and was poor in salts and in urea. French physicians tried to verify these assertions, and searched for the different modifications of the urine in chronic nephritis, aside from the presence of albumin. Rayer insisted especially

on the lowering of the figure for urea in albuminous nephritis; according to him, any dropsy accompanied by albuminous urine and diminished density, and especially diminution in urea, indicated with almost absolute certainty a renal affection. The opinions of Rayer were granted by most clinicians who studied this question; it became quite generally admitted that diminution in urea, diminution in salts, lowering of the density, were three factors which marched hand in hand with albuminuria in Bright's disease. To-day, the chemical composition of Bright's urine has almost entirely lost its significance; it is very difficult to deduce any clinical indications from the chemical composition of the urine.

Without stopping to examine in detail the changes which occur in the different substances (extractives and minerals) in the urine of Bright's (for in the present state of our knowledge such an examination has not much value towards diagnosis), we will only consider the modifications of the most important of the urinary constituents after albumin, and this is urea. It will be clearly apparent after we have studied it in the two opposed forms of Bright's, large white kidney and small red kidney, how restricted is its value from a diagnostic standpoint.

In parenchymatous nephritis the amount of urea is in direct proportion to the specific gravity of the urine; this is the richer in urea the less the quantity in which it is secreted. Such at least follows from the observations of Bartels.

At the beginning of the affection the quantity of urea is notably diminished, and this increases with the progress of the affection; the figure is always above the normal, oscillating usually between 12 and 15 gr., rarely exceeding 20 gr. (Charcot). Still, and this must be emphasized, the quantity of urea varies not only in individuals, but in the same patient both proportionately and absolutely (Bartels). It is evident, as justly states Labadie-Legrave, that in the Bright's patient with edema and abundant dropsical effusion the elimination of urea by the urine will be less active, since this product of disintegration escapes in part through the vessels with the effusions into the skin and the serous cavities; the same holds true for the subject to Bright's whose nutrition is compromised by abundant loss of albumin; in the latter, indeed, the proportion of urea and in consequence its elimination are restricted within appreciable limits.

If we compare these clinical facts with Lehmann's experiments it is easy to understand of what little importance is the quantity of urea excreted in parenchymatous nephritis. This observer has, indeed, proved that normally, under the influence of a simple modification in the diet, the quantity of urea may triplicate. How then take into account the variations of the urea in this affection? Likely enough the kidney plays a *rôle* in the small proportion eliminated, but the *rôle* is certainly a very secondary one.

Does the same hold true for interstitial nephritis? The study of the variations of urea in this form of Bright's is not more instructive; it is less, if this be possible.

For a long time the urea remains at its physiological height; the patient excretes from 25 to 30 gr. in the twenty-four hours (Bartels), a fact which is worth remembering. It is only later that the amount decreases to such a degree that we at times only find 1 to 3 gr.[106]

Under these conditions it is readily understood that daily dosage is of little value, and furnishes but few elements useful for diagnosis. This daily search, however, is not a useless one; if it does not assist in diagnosis it still furnishes the physician useful indications in regard to the nutrition of his patients.

Microscopic Characteristics of the Urine of Bright's.—If the chemical composition of albuminous urine has not much value from a diagnostic stand-point, the microscopic examination of the urinary sediment has not much more.

For a long enough time writers have attached great importance to the study of the urinary sediments, and especially of the casts; persuaded that they represented exactly the lesions of which the kidneys were the seat, they endeavored to distinguish carefully the different varieties, and they described in great detail the hyaline casts, the granular casts, the granular-fatty casts, the waxy casts, etc., each variety belonging to a determined renal lesion. Soon, however, it was ascertained that these casts were often found without the kidneys being much affected, so that they lost entirely in value. To-day they are hunted for rather as curiosities than as elements in the diagnosis. Still we must dwell on them a trifle, since, although they may be found in cases where the kidney is not affected, they are always found in case of chronic nephritis, and we may by their characteristics determine the variety of nephritis which is present.

In parenchymatous nephritis the urine is usually cloudy; the sediment is abundant and under the microscope are found crystals of uric acid, urates and phosphates, leucocytes, sometimes blood corpuscles, casts of varying kind and number. Bartels, who has made a careful study of casts, says: "The majority are pale, hyalin, or slightly striated, and often carry *débris* of epithelial cells. The more chronic the case the more frequent the granular casts, the larger they become and the more frequent the waxy casts."

In diffuse nephritis there is little sediment, and it contains fat cells and a few casts; not uncommonly there is no sediment for days in succession.

Casts are sparse in interstitial nephritis; microscopically a few crystals of urate and of oxalate of soda are found, and a few hyalin casts, exceptionally some granular. According to Robin[107] there is also found a notable quantity of urohematin. In short, the microscopic examination allows us to determine certain differences between the varieties of Bright's disease; but it is not necessary to hunt for casts in order to specify the variety of nephritis. To-day, therefore, the microscopic test is of restricted value.

Connection between Albuminuria and the General Condition.

Is it possible to deduce from the relations existing between albuminuria and the general condition data of utility from the stand-point of diagnosis of Bright's disease? This question we propose studying from a clinical stand-point.

In parenchymatous nephritis, together with the albumin which is present as a rule, we must note the edema which, in this affection, pursues a special course. At first transient and localized in the morning on the eyelids, at night at the malleoli, it soon becomes permanent and generalized over the body; its progress is peculiar enough to suggest the large white kidney even before the albumin appears to confirm the suspicion.

Although the diagnosis of this variety of chronic nephritis is usually easy, certainly, in the majority of cases, the same is not always true of renal sclerosis; the scarcely pronounced albuminuria, often absent, the slight dropsy, attract scarcely the attention of the physician when certain cephalic, digestive,

respiratory troubles lead into error. This he may often avoid by consulting the heart. The hypertrophy of this organ, so well described by Bright, is suggested to the ear by the *bruit de galop,* the characters of which have been well established by Professor Potain; but this valuable sign may be lacking and the diagnosis remain uncertain. Often still, in quite a number of cases, the attention of the clinician is attracted by special visual signs; a progressive amblyopia due to a retinitis of quite marked characteristics, leads to the thought of the possibility of an interstitial nephritis; therefore, in doubtful cases, an ophthalmoscopic examination should not be neglected. By never neglecting the data furnished by the heart and the fundus of the eye the diagnosis of renal sclerosis may often be established in its initial stage.

Although the special progress of edema allows us to suspect parenchymatous nephritis, and the heart murmur and the peculiar retinitis point to interstitial nephritis, affections which the albuminous urine in many instances will confirm, how much more difficult is it to make a diagnosis in all those obscure forms of Bright's so frequently met with, which are characterized, some by persistent headache, others by diverse sensorial troubles, others by dyspeptic trouble, others by a greater or less difficulty in breathing, others still by deep anemia, etc. If in these varied instances, so different the one from the other, the urine contains albumin, the diagnosis is, in general, easy; but if it be not present, how difficult the diagnosis! The diagnosis must be made, however (and this is essential both to the physician and the patient from the stand-point of treatment), it must be made, we repeat, and we must have the courage to order the rigid treatment required by such a diagnosis; cure, or, at most, rapid amelioration of the disease will soon justify the diagnosis.

To make the diagnosis in these difficult cases we must search with care for those little symptoms which our teacher has grouped under the generic name of lesser accidents of Bright's. cephalalgia; sensorial disturbances (buzzings, diminished vision, whistlings, more or less marked deafness, epistaxis in the morning); disturbances of the general sensibility; cramps; muscular twitchings; digestive troubles; respiratory troubles; urinary troubles.

All these accidents, which we can only mention, have, true

enough, only slight value when isolated; together they should lead to the right goal and should allow us to reach the diagnosis of Bright's even when careful repeated examination of the urine shows absolutely nothing abnormal.

We see, then, that it is not useless to study the general condition; careful search often gives valuable aid, not alone to complete the diagnosis, but in many cases to establish it with certainty.

Actual Diagnostic Value of the Symptom Albuminuria in Bright's Disease.

Having reached the end of the first part of our study it seems to us appropriate to resume our conclusions:

Albuminuria, abundant in the course of parenchymatous nephritis, is met with nearly constantly in this affection.

It is, on the contrary, rare in interstitial nephritis, in the course of which it occurs intermittently and is subject to great variations; in certain cases, even, infrequent enough to-day, but which will certainly soon become more frequent, albumin is entirely absent.

In the many varieties of diffuse nephritis its characteristics and progress vary greatly; we cannot, therefore, specify its principal traits.

In Bright's urine we do not always find a single and similar albuminoid substance; there are different varieties. One is met with constantly (serin), the others with greater or less frequency according to the case (globulin, peptones, propeptones).

At present we cannot infer anything to speak of from their presence or their absence; they neither specify the nephritides nor do they differentiate the clinical varieties.

The chemical composition of chronic nephritic urine has not the importance formerly granted it. The same is true of the characters furnished by the microscopic examination of the sediment, notably the casts.

The physical characters alone of the urine, although of less value than formerly, deserve recognition. The quantity of urine passed in the twenty-four hours not only allows us to differentiate the two chief varieties of nephritis, but it also

permits under conditions well specified by Lépine to separate the renal affection from those which may simulate it.

The general condition of the subject of Bright's must always be taken into account; it almost always furnishes useful information. The information indeed is often sufficient to allow us to affirm Bright's disease even when albumin is absent.

Finally, albuminuria has certainly a diagnostic value, but it is restricted enough when taken separately; its value is wider when considered in connection with the urinary secretion and the general state of the patient; we are then in a position, often, to affirm the renal lesion and to specify the variety.

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CHAPTER III.

THE PROGNOSTIC VALUE OF THE SYMPTOM ALBUMINURIA IN BRIGHT'S DISEASE.

At the outset of the first part of our study we deemed it useful to recall the phases through which the question of albuminuria has passed, in the belief that these historical considerations would enable us to rapidly arrive at the value of this symptom in the diagnosis of Bright's disease. To follow the same course here would be to lose time; indeed writers on this subject have paid but little attention to this point. In reading their monographs, although we find the prognosis of chronic nephritis well exposed, we meet with but few details in regard to the *rôle* which the symptom albuminuria plays in prognosis.

To take account of this *rôle* we must again study different factors: the existence and nature of albuminuria on the one hand, the connection between the urinary secretion and the general health on the other hand; in fact the same factors, the same examination, although more briefly.

Existence of Albuminuria.

The irregular progress, the frequent absence, the small usual quantity of albumin in renal sclerosis makes us think at once that in this variety of Bright's it would be very rash to attach much value to this symptom. Whence why all writers on this subject—Rayer, Charcot, Rendu, Rosenstein, Lancereaux, Bartels, etc., have not paid much attention to this point.

Lecorché, alone, suggests the prognostic importance of the presence of albumin in the course of interstitial nephritis. "When," he says, "the albumin is abundant (and this may happen at any stage of the affection) this is a sign that parenchymatous nephritis complicates the affection; the prognosis

becomes grave, for the loss of albumin is a further cause of weakness which soon leads to a condition of anemia."

Almost constant, notwithstanding its many variations, in parenchymatous nephritis, the albumin deserves serious consideration.

In general the presence of albumin in the urine has been always looked upon as a phenomenon of ill-omen; for the majority of clinicians, indeed, when the urine becomes albuminous the prognosis becomes very grave; as Bartels says, "if heat coagulates the urine in a test tube the patient is condemned."

Many, however, think that the unfavorable prognosis attributed to the symptom we are studying has been much exaggerated.

"Albuminuria is a bird of ill-omen in diseases of the kidney, to which an extreme importance is attached, behind which we expect the edemas and all the precocious or tardy symptoms of Bright's disease, and which are accused of provoking weakness. Still it is often a few centigrammes, at most a few grammes of albumin which the patient passes each day; such a slight spoliation is not capable of deteriorating the health. A nurse loses without harm 40 to 50 grammes of albumin or of proteid matter through the function of lactation and yet her health is not deteriorated." *

Is it really true that albumin must always retain its bad reputation? Or must we admit with Bouchard that it has been wrongfully accused?

To answer this question two points are, we think, to be considered: the quantity and the course of albuminuria.

Christison thinks that the greater or less amount of albumin cannot assist in prognosis. "The chances of death," he writes, "are not at all proportionate to the quantity of albumin in the urine. The reverse is true to a degree, for when albumin is abundant the organic derangement of the structure of the kidneys is in its first stage."

Rayer is not at all of this opinion, and looks upon abundance of albumin as an unsavory phenomenon; such at least is the conclusion to which his numerous observations have led him.

Since, the majority of writers have considered the abundant

* Bouchard: Auto-Intoxication dans les Maladies, 1887.

loss of albumin as grave; but have attached a greater or less importance to it.

"The prognosis is serious when persistently the urine contains a large amount of albumin, for every circumstance which increases the organic loss at the expense of the vital resistance constitutes but another unfavorable condition." (Rendu.)

"If the renal affection is accompanied by fever or by other phenomenon which interferes with nutrition and repair, the great albuminuria becomes a cause of weakness, even as does an abundant leucorrhœa, dysentery, suppuration, frequently evacuated ascites. An abundant albuminuria may cause impoverishment of the blood." (Bouchard.)

The abundance of albumin is, therefore, a point to be considered; it furnishes, indeed, certain useful information.

Much more interesting, however, is that furnished by the progress of albuminuria in parenchymatous nephritis.

During the evolution of this affection, on which we have dwelt at length, occur two kinds of variation, which are far from being of the same importance.

The first which occur from day to day appear without known cause; more or less frequent according to the case, they are not accompanied by any change in the health of the patient. They must be recognized, however, since for long it was thought that an increase or diminution in the albumin was regularly in accord with aggravation or amelioration of the other symptoms. In looking over the cases of Rayer we find a number of quite marked cases. This is far from being the rule; therefore, in general, to base a prognosis, of one sort or another on the increase or the diminution of excreted albumin, would be *à priori* to run the risk of great error.

But although these daily variations have not the same importance that were formerly attributed to them, the same does not hold true of the changes occurring regularly from time to time. These are generally consecutive to treatment. We will dwell on them for awhile.

When a subject to Bright's is placed on milk diet a number of things may happen:

Sometimes the albumin, after having progressively diminished from day to day, disappears entirely from the urine. This disappearance is complete and certain when, the patient having been placed on ordinary or mixed diet, the albumin

does not return; the prognosis here then is eminently favorable. It is less so when the suppression of the milk and the return to ordinary diet is followed by a sensible and persistent increase in the amount of albumin. Truly, while in the first instance we may look upon the patient as completely cured, we must, in the second, consider him as having still a nephritis in the stage of evolution and we should prepare for the accidents which occur so frequently in the course of parenchymatous nephritis.

Again, after having progressively diminished for a greater or less time, the albumin remains stationary. The patient has 1 to 2 grammes of albumin, oftener only a few centigrammes, or even only traces. What should be the prognosis in such a case, so frequently met with?

Although many clinicians claim that we ought not to admit a cure of the disease until the albumin has entirely disappeared, there are others who believe that we need not attach to the presence of this substance such great prognostic significance; as a proof of what we say we will quote the following passages from two writers who have made a special study of chronic nephritis:

"While albumin remains in the urine, even in small amount, even though all the other symptoms have disappeared, we must not fall into error, for the property of this disease is to present in its course the most marked oscillations and it is not rare to see the albumin increase at the same time that the other symptoms reappear." (Lecorché.)

"If," says Jaccoud, "suppression of milk diet and drugs and return to ordinary diet, are not followed by any variation in the albumin, and this for a number of consecutive months, the patient may be considered cured, notwithstanding the persistence for an indefinite time of a few centigrammes or of traces of albumin. Without question this patient is more subject to nephritis than another, and should take special precautions against cold, dampness and errors in diet, as also abuse of alcohol and exercise; but with regard for these rules he retains his health notwithstanding the presence of this insignificant amount of albumin. I have seen after the lapse of 3, 4, and 5 years patients thus cured up to a few centigrammes, and I have found that they retained their health notwithstanding this remnant of albumin."

Finally, at times, the amount of albumin does not vary or varies but little as the result of treatment and remains considerable. The prognosis is grave, not because a large amount of albumin is excreted daily, but because this amount indicates that the kidneys are markedly affected; and we know from the researches of Brucke that it is the extent rather than the depth of the lesions which renders parenchymatous nephritis grave.

A consideration, then, of the existence, quantity and variations of albumin gives, in case of the large white kidney and of mixed nephritis, useful information. It is not, however, sufficient to allow us to base on these data alone the prognosis of the disease. We must join other factors, to which we now pass.

Connection of Albuminuria with the General State.

In case of Bright's we must never neglect to inquire into the general health. The latter, in general, behaves as does the albumin, becoming worse as it increases, and better as it diminishes. There are, however, certain exceptions worth noting:

Often we see, notwithstanding a marked diminution in the albumin, the general health remains bad; in the presence of these facts we are forced to admit that the disease runs its course; the prognosis should be greatly reserved. Certain symptoms may, however, persist without aggravating the prognosis; thus it is not rare to find in pale and anemic subjects a persistence of dropsy after complete disappearance of dropsy. We may still believe in complete cure of the affection and give a prognosis accordingly. (Lecorché.)

Again, and the cases are frequent, the patient seems to have recovered his health and the albumin persists; we have sufficiently insisted on this point.

We see then that albuminuria and the general state are subordinate the one to the other, and that we must always consider them together if we wish to establish a certain prognosis.

Connection of Albuminuria with the Urinary Secretion.

The relations existing between albuminuria and the urinary

secretion also play a certain *rôle* from the stand-point of prognosis which it is of importance to recognize. For the sake of completeness we must pass successively in review the physical, chemical and microscopical characters of the urinary secretion.

Physical Characters.—Rayer has chiefly studied this question, and we borrow most of our details from his work.

From a physical stand-point two characters of the urine are to be considered: the quantity of urine and the specific weight.

The quantity of urine passed is certainly important to consider; but it is difficult to trust the deductions thence drawn. Notwithstanding every precaution the patients often lose a part of their urine. If, however, we can measure the exact amount we can consider to advantage the progress of the secretion.

An increase in the amount of urine in the twenty-four hours, aside from the drink taken, is a good sign, especially when this increase coexists with diminution of the dropsy and the albumin. This increase may, however, be transient, and may be soon followed by a more or less marked arrest in the secretion, which is an index of increase in the symptoms.

Diminution in the amount frequently foretells an increase in the existing dropsy or the appearance of dropsy.

When the diminution is more marked, and, of course, when there is complete suppression, the prognosis is very grave; for this indicates the approach of cerebral symptoms.

The specific gravity is also of value, for it furnishes valuable information.

When the density increases, and this is due to an increase in the salts, especially of urea and the extractives, the prognosis is very favorable. This, however, rarely happens.

When the density diminishes, the sign is a bad one if the amount of urine secreted is not increased, and if the amount of albumin remains stationary

Microscopical Characters.—To these characters much consequence was formerly attached, but to-day they do not possess much importance. We will not dwell on them.

The Chemical Characters.—Urea has for long played the chief *rôle* in the chemical constituents of the urine.

"A notable diminution in the urea is a bad sign, whether it co-exists with an abundant albuminuria or not; for in these cases death has frequently followed quickly on cerebral accidents." (Rayer.)

Lecorché and Rendu are not less categorical:

"The diminution in urea is a sign of such value that it answers for making a very grave prognosis if the albumin has also diminished."

"The danger is all the greater if the urea is eliminated in great abundance and the alimentation remains stationary."

The important *rôle* granted urea has been much exaggerated: "For long considered as the great poison, urea is not specially toxic." (Bouchard.) He shows, indeed, "that solutions of urea only cause death when injected in the strength of more than 1:2 c.c. to the kilogramme of the animal, a dose at which pure water kills."

The toxic agent is not the urea, but the total amount of the excrementitious substances contained in the urine.

Professor Jaccoud has held the same view for twenty years. In his lectures at the *Charité* in 1867 he showed that uremia was not due to the accumulation of urea in the blood, but of the materials of the urine. The urine is then toxic, not because it contains a greater or less quantity of urea, or of other element, but it is toxic in totality.

In view of the toxic power of urine it was of the highest importance to find out the nature of the toxic agent in Bright's disease, since, as our teacher says, "in this affection the point of ill-omen is not what happens, but what does not happen."

What matter if the patient passes a greater or less quantity of albumin or of urea? What is of importance is to know how the diseased kidney functionates; what, in other terms, is its degree of permeability. Does the kidney in twenty-four hours eliminate the amount of poison which the organism manufactures in twenty-four hours? This is the question to be answered before we can make our prognosis.

This question is readily answered by seeking in a given case the degree of toxicity of the urine.

Professor Bouchard has shown in his experiments that the amount of poison necessary to kill a kilogramme of a living being, the urotoxia as he calls it, is on an average 50 c.c. of urine, the mixture of twenty-four hours. This fact having been established after the most positive manner, we can readily take account of the urinary toxicity, and in consequence judge the state of the kidney.

Basing his researches on the discovery of Bouchard's, our

teacher has determined time and again the toxicity of the urine of Bright's. We reproduce the following determinations, which seem to us conclusive enough:

Case XIII. (*Abstract.*)

Bright's Disease.—Absence of Albumin.—Feeble Toxicity of the Urine.—Patient æt. forty entered hospital for lumbar and abdominal pains; for some time she has had sensation of "dead finger," cramps and pollakiuria. The diagnosis of Bright's was made by Dieulafoy.

The quantity of urine varied from 1200 to 1400 c.c., and it was poor in urea and in salts of potass; it contained no albumin.

A rabbit of 2 kilo. was taken; 80 gr. injected caused dyspnea and tremor; 90 gr. myosis; 150 gr., salivation, exophthalmia, convulsions; 125 gr. abolition of ocular reflex; 130 gr. convulsive movements of the masticators, and of the neck, respiration almost abolished; 160 gr. death.

The rabbit should have been killed by 100 gr. of normal urine; 160 gr. killed it; the urine of this patient was less toxic than normal urine.

Case XIV. (*Abstract.*)

Bright's Disease.—Absence of Albumin.—Very slight Toxicity of the Urine.—Patient æt. forty-two, admitted May 8th, violent cephalalgia.

Her symptoms dated back four years when, without appreciable cause, edema of the feet and legs, headache, lumbar pains, cramps, and dyspnea, set in. At the end of three months this group of symptoms had about disappeared. At the end of two years cephalalgia, visual and auditory symptoms; precordial pains, lumbar pains, set in. The urine was about normal in quantity, poor in urea and in salts of potass; for twenty six consecutive days no albumin.

Rabbit of 2 kilo. taken; 230 gr. injected caused dyspnea, myosis and prostration; at 260 gr. the rabbit could not hold up its head, in ten minutes it had diarrhea and abundant micturition; it shook its head, walked a trifle, and in a half hour was itself again.

This animal should have been killed by 100 gr. normal urine.

Case XV. (*Abstract.*)

Bright's Disease.—Absence of Albumin.—Feeble Toxicity of Urine.—Entered hospital for intense cephalalgia, which had lasted for a number of years. Two years previously had had anasarca, dyspnea and whistlings in ears. Three months

ago there had appeared cramps, pollakiuria, "dead finger," etc.

No albumin in urine. Into a rabbit of 1995 gr. 97 gr. urine was injected without symptom.

285 gr. was necessary to kill a rabbit of 2.210 kilo.

We would add further that the urine from non albuminuric Bright's (*vide* our observation No. 5) was also non-toxic; 260 gr. were needed to kill a rabbit of 2700 gr.—that is to say, exactly double the quantity of urine.

From these experiments there follows the following fact: generally the urine of patients supposed to be Brightic, and yet non-albuminuric, is less toxic than normal urine.

Similar experiments were made by our teacher in case of Bright's with albuminuria, but we cannot as yet state the deductions.

The above experimental method is of great interest; if at times it may be very useful from the stand-point of diagnosis, it is always useful from that of prognosis, since it allows us to judge quickly as to whether the urinary depuration occurs or not.

Such experiments, however, we must emphasize, prove but one point: this is, that on the day or days when made the urine was or was not toxic. To go further than this would be, it seems to us, to fall into great error. To state positive conclusions it is necessary to examine the urine in question every day. There are disadvantages in this, however; in the first place such experiments take time, and in the second place they are quite expensive.

The discovery of Bouchard's, however, is most important. In order to reach a prognosis we must, in particular, base our opinion on the toxicity of the urine.

If the urine is not toxic the elimination is incomplete; the kidney does not functionate, it is certainly more or less altered in structure.

If the urine is normally toxic, the urinary depuration is complete; the kidney functionates regularly; the affection, if not cured, is at least much ameliorated

Nature of Albuminuria.

There is one matter which so far we have left in the shade, and this is the question of urinary albumins. This question is

in dispute. The diagnostic importance is little known, and their prognostic is less known. We only know that serin has pathological importance; the other albumins are only the indices of a non-determined modification of the blood. (Jaccoud, Lépine.) They furnish absolutely no information from the stand-point of prognosis.

We believe, however, that when we have become familiar with the search for these albumins, and when we have carefully noted the conditions under which they appear, we may draw useful deductions; we may then be able to follow quite precisely the progress of the renal lesion.

Actual Prognostic Value of the Symptom Albuminuria in Bright's Disease.

We draw the following conclusions:

For a long time, in order to reach a prognosis in Bright's disease, the existence, the progress, the variations of albuminuria were taken into account, as well as its connection with the general health and the condition of the urinary secretion.

These characters allow us, true enough, in certain cases to reach a prognosis, especially when the *ensemble* is considered; they are, however, insufficient to enable us to judge the question definitively.

We know, to-day, that the prognosis depends on the permeability of the kidneys; we must know in order to reach our prognosis, whether the kidneys allow or not of the complete elimination of the toxic matters manufactured by the organism.

This search must be made repeatedly to enable us to reach any conclusion.

Later on, perhaps, we may be able to judge the question more readily by taking into account the nature of the excreted albumin. If this supposition is confirmed, and it seems to us likely, we will have at our disposal a more practical method than the daily examination of the toxicity of the urine.

CHAPTER IV.

CONCLUSIONS.—ACTUAL CLINICAL VALUE OF ALBUMINURIA IN BRIGHT'S DISEASE.

Having passed in review in as detailed a manner as possible the various factors which may give us information in regard to the nature of albuminuria, we believe we are in a position to answer the question we proposed for solution. We may, indeed, actually fix the clinical value of the symptom albuminuria in Bright's disease.

We need recall here only the salient conclusions which may be deduced from the study.

The clinical value of the symptom albuminuria in Bright's, whether considered from the stand-point of diagnosis or of prognosis, is rather restricted; in order to affirm the renal affection, in order to state its progress and consequences, albuminuria may answer, but not alone.

Whatever the case, it should be recognized, for it furnishes valuable information.

If in many cases albuminuria, by its progress and characteristics, enables us certainly to recognize and to affirm Bright's disease, and often indeed to state the variety, there are other cases, also numerous, where its absence or its inconstancy would lead us into error, if we could not depend on information drawn from the urinary secretion and the general condition. Albuminuria, then, has a certain diagnostic value, but too often restricted if considered alone.

Its prognostic value is much less; to depend on it alone is altogether insufficient: to the information it gives us must also be joined that furnished by the urinary toxicity, which for the present must remain the great prognostic criterium.

To conclude: In Bright's disease, albuminuria has but a secondary value, at least in a large proportion of cases.

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